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Neural substrates underlying planning interactions with bimanual tools: a functional magnetic resonance imaging study

Neuronalne podłoża planowania interakcji z narzędziami dwuręcznymi: badanie z wykorzystaniem funkcjonalnego rezonansu magnetycznego

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Introduction

"*As is obvious from patients with movement disorders, neophyte performers, and most modern robots, motor control is far from a trivial problem.*"

Rosenbaum, Van Heugten, & Caldwell, 1996, *Acta Psychologica*

"*One of the most impressive features of human beings is their ability to produce a bewildering variety of coordinated behaviours that involve the upper and/or lower limbs.*"

Swinnen, 2002, *Nat. Rev. Neurosci.*

Most of our numerous daily activities are performed with both of our hands. Despite the fact that such actions require quite complex neural computations, most of the time we are not even aware how sophisticated sequences of movements are needed in order to carry out such tasks. Yet until now, at least in the context of tools, researchers studied mainly quite simple activities, such as lifting up and using the hammer, writing down a note with a pen, or sweeping the floor with a brush. Regardless of whether we use one or both hands in a coordinated manner, we tend to realize how well-orchestrated movements are required only when something goes wrong. That is to say, we notice the involved action-related complexities only when we make mistakes, e.g., during handling too many things at a time, or we end up dropping our favorite plate. Alternatively, when we get injured or we feel a substantial pain in either of our hands or arms, we lose the ability to properly use one or both of our upper limbs. Then we quickly realize how important coordination of both arms (hands, wrists and two sets of fingers with opposable thumbs) is to our daily functioning.

Evolutionary speaking, our tremendous manipulating capabilities give us an advantage over even stronger, more physically potent species. In their case, coordination is typically associated with the control of locomotion, e.g., movements while running, or jumping from branch to branch. In the human beings, on the other hand, performing sequences of coordinated movements also allows for creating and using tools, with which we are able to shape the surrounding environment in ways that extend nature-given possibilities of our organisms. With theoretical and technological advances, there emerged an opportunity to better understand the biological basis of tool-related behavior. In particular, the adaptation of neurophysiological methods to studying psychological phenomena, such as planning and intentional control of actions, brings us closer to resolving centuries-old disputes about how the external world is

represented and processed by our organisms, with particular interest lying in the activity within the central and peripheral nervous system.

Authors in the field of neuroscience and psychophysiology have been studying tool actions and cognition for over a hundred years now. Still many questions are left unanswered and hypotheses untested. However, what is generally agreed upon is that the preparation and control of tool-related actions (i.e., grasping and using tools accordingly to their afforded functions) is governed by the so-called *praxis representation network* (PRN). Nevertheless, for various reasons, the vast majority of classic paradigms, as well as modern neuroimaging studies, either considered only actions towards tools that could be handled with just one hand, or did not differentiate between unimanual and bimanual manipulations at all.

The contribution of my thesis to the almost three decades of functional magnetic resonance imaging (fMRI) research on skilled actions shall reveal numerous preparatory neural mechanisms that must occur prior to the integration of complex and coordinated movements of both upper limbs, a process necessary for adequate interactions with bimanual tools. It turns out that this seemingly straightforward category of actions requires neural computations from various regions across the brain, including an interhemispheric communication between its two cerebral hemispheres. Such communication is a prerequisite of skilled tool use, not only when a tool is directed at different object, but also when two functional parts of a single tool are handled by two hands, or two supporting tools are needed in order to perform a single task. Moreover, the two hands can play various roles in bimanual tool use: either both play corresponding roles in a synchronized manner, or one is dominant and the other supports or mediates the performed action.

Although bimanual coordination has already been quite extensively studied, never before have the questions been asked about how the adult human brain prepares for proper grasping and acting upon the very peculiar categories of objects, such as bimanual tools. These interactions require not only proper, even if sometimes simple, grasping and/or transportation movements, but the associated actions have to be functionally adequate, and they have to be followed by more refined sequences of relevant movements. In the light of recent results from studies on preparatory grasp mechanisms, the fact that actions consist of distinct phases cannot be underestimated, either. In other words, the monolithic approaches to studying processes underlying interactions with tools should be abandoned in favor of multi-phasic or continuously interchanging stages of information processing within neural subnetworks distributed across the brain.

Chapter 1. Background of the study

In the following sections the necessary terms regarding the planning of bimanual grasps of tools will be introduced and defined, with an emphasis on bimanual coordination and movement transformations. Afterwards, the relevant literature will be presented, with studies categorized in terms of their theoretical framework, and the experimental method/paradigm type. Finally, at the end of this chapter the ideas behind the current project will be described in more detail.

1.1 Definitions of skillful tool use and functional grasp

It is not clear as to when our the so-called *material culture* (focused on tools and other artifacts) had its beginnings. Yet, it is already known that Plio-Pleistocene hominids were already using simple stone and non-stone objects as tools (van Schaik, Deaner, & Merrill, 1999). Depending on the exact definition of "*a tool*", it can be said that primates were able to manipulate objects in a tool-like fashion even before the phylogenetic separation of the *homini* taxonomic tribe (and the subsequent emergence of the *homo sapiens* species). Nevertheless, due to the extent and frequency of behaviors concerning crafting and using tools among our species, this fascinating phenomenon requires more in-depth studies, and many questions are yet to be addressed, while new issues arise as our own evolution progresses.

From the neuroscientific perspective, using tools in a functional way, i.e., accordingly to their purposes, requires parallel signal processing in numerous, highly specialized brain areas. The neural computations that allow us to correctly grasp and use tools have been extensively studied in the past by various groups of researchers (Buxbaum, 2001; Castiello, 2005; Johnson-Frey et al., 2005; Orban & Caruana, 2014; Vingerhoets et al., 2013). According to their reports, the burden of grasp-preparatory processing falls on the *praxis representation network* (PRN). Etymologically speaking, *praxis* refers to the process of using theory in practice (as defined in the Cambridge Dictionary[1]), but for the purpose of this thesis, its definition includes skilled (learned) sequences of physical actions/movements. In the literature on neural underpinnings of manual praxis skills, PRN is usually defined as a left-lateralized temporo-parieto-frontal set of brain regions and sites responsible for the retrieval of knowledge on actions, and the planning of complex manual movements necessary for efficient tool use (cf. Frey, 2008; Kroliczak & Frey, 2009). More recently, Przybylski and Króliczak (2017) demonstrated, however, that even

[1] Praxis definition: https://dictionary.cambridge.org/dictionary/english/praxis

planning of a simple function-oriented grasp (not the usage *per se*) elicits changes in neural activity within this network (as compared to control non-tool objects; see Przybylski & Kroliczak, 2017). This suggests that such neural changes depend on object *affordances* (Gibson, 1979), and that the underlying computations are contingent on the processing of visual information within the PRN, and the retrieval of action concepts.

In a broader context, the perplexing nature of the human-unique phenomena of intention-driven skilled manual movements has been puzzling researchers for over a century now (Goldenberg, 2003). Numerous studies addressed various aspects of information processing within the PRN in order to reveal the factors modulating activity patterns within this set of brain regions. Among the factors worth mentioning here are: tool complexity (Frey, 2007; Raś, 2020), whether tool use is real or pantomimed (Hermsdörfer et al., 2007), demonstrating vs. pantomiming tool use (without the actual target recipient; Lausberg, Kazzer, Heekeren, & Wartenburger, 2015), and the availability of the object within the peripersonal space (e.g., whether a tool is within a reach or not; cf. Gallivan, Cavina-Pratesi, & Culham, 2009). Additionally, to a lesser extent, the to-be-used hand may also play a role in preparing and executing a functional grasp (Choi et al., 2001; Kroliczak & Frey, 2009; Przybylski & Króliczak, 2017). Furthermore, using consequently the same effector can be more computationally efficient, and will results in faster reaction times (Valyear & Frey, 2015). Finally, handedness is sometimes also mentioned as a factor significantly explaining the variance in the signal observed during performing skilled manual motor sequences (Jastorff, Begliomini, Fabbri-Destro, Rizzolatti, & Orban, 2010; but cf. Kroliczak, Piper, & Frey, 2016).

While studying *praxis*-related literature, one therefore has to appreciate the advances in this field contingent on the plethora of studied conditions that, no doubt, influence the underlying neural processing for skilled performance of manual tasks. Nevertheless, the question to be addressed in the context of planning functional grasps is how the information processed within the brain contributes to bimanual, as compared to unimanual, tool use.

1.2 Bimanual actions

In nearly all of the previous reports on PRN the studied phenomena involved almost exclusively the use of *unimanual* artifacts – such as tools, or natural objects. However, if we consider our daily experience, it turns out that there are plenty of objects that need to be grasped and used bimanually in order to exercise their functions (van Elk, van Schie, & Bekkering, 2014; for the excellent remark on the evolutionary context of the relation between bimanuality and its neural

underpinnings, see Glover 2014). Moreover, while bimanual actions themselves have been in the scope of extensive research for almost four decades now (Shea et al., 2016), the focus was mainly on simple actions, such as coordinated finger movements (Mechsner et al., 2001) or drawing (Summers et al., 2008). Further attempts in studying bimanuality have been already made for chimpanzees and baboons (Hopkins et al., 2001, 2011; Miller et al., 2017; van Schaik et al., 1999; Vauclair et al., 2005). As a matter of fact, also the link between ambidexterity (when using both hands) and bipedality was observed in chimpanzees – the more demanding the task is, the more probable the subject was to use only one hand (the right one; see Braccini et al., 2010). As it turns out, many questions regarding the neural underpinnings of coordinated bimanual actions involving functional objects in humans still need to be answered, and some of the most crucial hypotheses will be presented later on in the following subsections.

1.2.1 Bimanual coordination

In a broader context, manipulation of bimanual tools may be classified into a wider class of movements, namely, bimanual coordination. Theories on bimanual coordination utilize paradigms ranging from simple manual movements (performed with bare hands – see Brandes, Rezvani, & Heed, 2017; Mechsner et al., 2001; for a comprehensive model of coordination dynamics – see also Haken, Kelso, & Bunz 1985), through tasks such as drawing (Summers et al., 2008), or object manipulation (Berger et al., 2018), up to the functional use of "everyday" tools (see a previous section, as well as: Massen & Sattler, 2010a, 2010b). Notably, more complex sequences of movements were explored with behavioral paradigms in works by Michel and collaborators, where the authors studied developmental aspects of acquiring the ability to perform bimanual operations on objects such as tool-toys or non-functional objects (see Babik & Michel, 2016; and Michel, 2018). In this line of research, one hand plays the dominant role during performing an action, and – as the *role* of each effector differs – the other hand plays a supportive *role*, and the relevant hand selection is thought to depend on the subject's *preferences*. This phenomenon is referred to as role-differentiated bimanual manipulation (RDBM). Babik and Michel, considering previous reports on this subject, pointed out that coordination of bimanual movement requires, among other things, collaboration between left and right brain hemispheres (Babik & Michel, 2016). Interestingly, hand preference for RDBM seems to be preceded by a development of hand dominance for unimanual manipulation, that, in turn, requires the hand preference for object acquisition to be established.

What could be added to this theoretical debate is the fact that a *role* that each hand plays during bimanual manipulation, especially the role of the non-dominant hand, may substantially differ. Namely, according to the most common definition of bimanual manipulation, one hand takes *the active, dominant role*, while the other just *controls* or *supports* the action (Babik & Michel, 2016; Serrien et al., 2006). Meanwhile, we may well think of the situation where both hands perform *active* manipulation. In fact, this phenomenon is the subject of most of the behavioral bimanual coordination paradigms mentioned earlier. Even in our daily activities we may find examples of such manipulations, e.g., when we are rolling pastry or trimming a hedge. Having said that, the scenario in which the non-dominant (or *non-preferred*) hand simply supports its *active* counterpart resembles to some extent unimanual manipulation, in contrast to a situation in which both effectors play *an active* role.

Numerous behavioral studies on synchronization of upper limb movements are the primary source of knowledge on this phenomena (see, e.g.: Brandes et al., 2017; Massen & Sattler, 2010a, 2010b; Mechsner et al., 2001; Summers et al., 2008). In addition to these behavioral paradigms, various neuroimaging methods and techniques of data analysis are being utilized to study bimanual coordination. The two main approaches are: brain oscillations, measured with electroencephalography (EEG; for example the work by Berger and collaborators, 2018), and functional magnetic resonance imaging (fMRI; e.g., reports by Sun, Miller, Rao, & D'Esposito, 2007 and Vingerhoets et al., 2012). For three excellent reviews on the neural underpinnings of bimanual (or *intermanual*) coordination, the reader is referred to works by Swinnen (2002), Carson (2005), and Shea et al. (2016). Furthermore, an in-depth discussion on some aspects of bimanual coordination in the context of lateralization of functions, interhemispheric communication and integration of information across the two brain hemispheres can be found in a paper by Serrien, Ivy and Swinnen (Serrien et al., 2006).

What is also worth mentioning here is that the report by Riccardi and collaborators (Riccardi et al., 2020) suggests a possible link between praxis skills and knowledge about how to manipulate objects. Their study revealed that lesions within PRN can be associated with disturbed semantic knowledge and comprehension of manipulable nouns (Riccardi et al., 2020). Moreover, the authors noted that the same frontal regions, which are damaged in stroke patients that have worse manipulable noun comprehension, are also engaged in: "*motor planning, execution, observation, and visuomotor coordination, especially pertaining to hand-related actions (Caspers et al., 2010; Binkofski & Buccino, 2006; Rizzolatti, Fogassi, & Gallese, 2001)*". Thus, either knowing how to manipulate objects (manipulation knowledge) is necessary for skillful object use (praxis), or it is a separate brain mechanism which supports

using functional objects, but is not one of the key factors driving this ability. (For the distinction between manipulation knowledge – knowing "what for", and function knowledge – knowing "how" see Boronat et al., 2005.)

1.2.2 From movement trajectories to brain-computer interfaces

The bimanual action coordination phenomena can be also considered from a perspective revealing the principles of transformations of movement trajectories for both hands simultaneously. This, somehow more of an engineering aspect of interacting with tools, is being intensively studied in the context of brain-computer interfaces and neuroprosthetics (Andersen et al., 2004; Carmena et al., 2003; Pistohl et al., 2012; Schaffelhofer et al., 2015; Taylor et al., 2017; Wang et al., 2019; Wessberg et al., 2000). For instance, Pistohl and collaborators successfully decoded different kinds of grasp (precision vs. power grasps) from the human motor cortex (Pistohl et al., 2012), while Schaffelhofer and colleagues (2015) found that many different kinds of grips performed by rhesus monkeys are represented not only as individual movements in animals' (pre)motor cortices (i.e., "*joint angle control"*) but also in higher-level cortices (Schaffelhofer et al., 2015). Interestingly, as grasps can be *decoded*, there have to be brain mechanisms for *encoding* these specific interactions with objects. However, studies on these mechanisms do not provide convincing evidence for explaining the nature of this encoding. In fact, BCI research is mostly concerned with the pragmatic context of the movement control, e.g., the usefulness of recreating complex sequences of hand trajectories in a remotely controlled robotic arm (Andersen et al., 2004; Kang & Ikeuchi, 1997, 1994; Kragic et al., 2015; J. Lee et al., 2012; Lin & Sun, 2015). The general procedure for that is: recording patterns of neural activity in motor and/or premotor cortices, and analyzing the signal, for this input to be further used to control the robot, with little concern for the origin of these signals in the brain. Although from this perspective the subject seems like more of an engineering issue (as the agent's "*motor commands for producing movement*" are not of a major significance here), it is worth trying to comprehend the potential contributions of this approach to cognitive neuroscience. Namely, transcribing the discussion on the *lower level* of neural processing and referring to *movement trajectories* and *control commands* allows us to avert many misinterpretations and misunderstandings that we are prone to when we operate with the semantically wider terms such as *action intentions*, *reach goals*, etc. However, one has to be cautious not to lose the *cognitive* aspect of the studied actions, as well (for a discussion, see Osiurak & Danel, 2018, and Mangalam & Fragaszy, 2018).

Inspecting this issue further, one may notice that there also exists a specific line of research dedicated to designing and testing robot-based solutions that assist bimanual movement coordination for the purpose of post-accident and/or post-stroke motor rehabilitation (Herrnstadt et al., 2015; Lewis & Perreault, 2009; Lowrey et al., 2014; Nordin et al., 2014; Trlep et al., 2012). To provide a quantitative assessment of post-stroke rehabilitation, Lowrey and collaborators (2014) developed a robotic task which may in the future be used alongside or instead of standard measures that require more time and effort from the side of health practitioners. There were also attempts to reverse-engineer human bimanual movements to optimize robotic movements (Gribovskaya & Billard, 2007; Lee et al., 2012). It is worth noticing that coordination of movements is not restricted exclusively to upper limbs. Fitzsimmons and collaborators decoded several kinematics' parameters of bipedal walking from the rhesus motor cortex (Fitzsimmons et al., 2009). If these results could be obtained for non-overt movements, brain-machine interfaces utilizing this technology could possibly be used to facilitate restoring walking in paralyzed patients.

Yet another example, where potential differences in movement kinematics were accounted for is a work where two qualitatively similar tasks were examined, such as writing letters and writing digits (Longcamp et al., 2014). As it turns out, for these two kinds of manual actions (very similar in terms of the movement kinematics), separate neural representations were distinguished with fMRI in healthy participants. These findings are supported by observations from neuropsychological research (see Anderson, Damasio, & Damasio, 1990). In a similar vein, kinematics were also used to explain the implicit component of motor sequence learning (Swett et al., 2010), sport-related anticipation (Wright et al., 2011), and interhemispheric competition (Nowak et al., 2014).

As presented above, the phenomena of coordinating hand movements can be analyzed at either of the two levels: higher, wherein patterns of brain activity reflect some general manual task, or a lower one, with kinematics, trajectories, transformations and their direct relation to specific neural processing. By "higher level" I understand approaches where probabilistic measures are employed to model the relation between internally-driven behavior and the underlying neural activity that was necessary to plan and execute a given action. On the other hand, if we consider arm, hand or finger movements as physical bodies/objects changing their location in space, these movements may be thought of as a result of object orientation, acceleration, vector, velocity, and the number of the degrees of freedom of these physical objects. These spatial dependencies can be modeled mathematically (geometrically) as transformations: translation and rotation, where physical quantities such as vector, speed

(velocity) and acceleration would then be a function of time of transformation operations. Of course, it is possible to incorporate these two approaches into one, coherent model, in which the neural representations of spatial features of hand movements are to be revealed and explained (e.g., Casellato et al., 2010; or Gassert et al., 2006).

1.2.3 Earlier studies on interactions with bimanual tools

Yet another interesting aspect of bimanual actions is their role during observing our conspecifics performing such actions, and the neural underpinnings that are associated with this observation. There is some evidence that, although the mechanisms behind action observation are well characterized, there is no answer as to how neural representations of bimanual actions differ from those of unimanual actions (Heitger et al., 2012). To address this issue, Heitger and collaborators came up with a paradigm, in which participants watched an actor performing the following actions: (1) bimanual, (2) unimanual with the right hand, and (3) unimanual with the left hand. FMRI signal acquired during watching videos with these conditions was contrasted with corresponding control conditions – spheres with black and white patterns, whose movement accounted for motion kinematics (an approach inspired by Jastorff et al., 2010). Subsequently, the outcomes of these contrasts, corresponding to bimanual and either of the unimanual conditions, were compared to each other. In other words, two comparisons were performed: (1) [(bimanual action – bimanual control) – (unimanual right hand action – unimanual right hand control)], and (2) [(bimanual action – bimanual control) – (unimanual left hand action – unimanual left hand control)]. According to the authors, using interaction tests rather than simple subtraction can reveal an effect independent from the processing of lower-level visual features of motion. Although there was no consistent interaction effect across hands, bimanual actions yielded 3 statistically significant sites when compared to unimanual left-hand actions: right middle medial intraparietal sulcus (mmIPS), left posterior middle temporal gyrus (pMTG), and right occipital cortex (OC). Nevertheless, the authors noted that there are some differences in activations between observing bi- and unimanual manipulative actions – not in which brain regions are activated, but rather in how the activity is bilaterally distributed. Namely, the activity was more balanced in bimanual condition, which comes down to the question of the differences in the lateralization of bi- and unimanual actions – the issue that will be raised further on. Notably, one the factors Heitger et al. did not consider was the fact that some objects used in stimulus movies were natural objects (e.g., grapes or bananas), and other were artifacts (such as bottle or peanut box). However, there are convincing pieces of evidence that these two categories of objects – tools (artifacts) and natural objects – are

processed differently within the cerebral cortex (see Gough et al., 2012). Thus, this issue should be carefully controlled in further studies, with the use of even more sensitive paradigms (e.g., event-related design).

Although from cases of the apraxic patients it is known that learned movements of both hands are mostly left lateralized (e.g., Petreska, Adriani, Blanke, & Billard, 2007), the degree of praxis lateralization for bimanual actions remains uncertain, as these patients often experience post-stroke motor problems with a limb contralateral to the hemisphere where a stroke occurred. Another issue is that the lateralization of motor acts is by itself dynamic and may vary within particular time frameworks (Serrien et al., 2006). For instance, when learning a new, demanding bimanual task it is the right-hemisphere that is initially being more active (Swinnen, 2002). Over time, this right-hemispheric activity can diminish, and the increasing automation of movements is represented mostly in the left hemisphere. Moreover, it might be the case that disparate kinds of skilled manual behaviors are lateralized somewhat differently, and/or the processing may be more balanced across hemispheres (see the study by Heitger et al., 2012 mentioned above). To sum up, although praxis itself is usually a strongly lateralized ability, the lateralization of motor control of bimanual actions can vary and it is most probably dependent on the interaction of number of conditions. Hence, in order to address the issue of laterality of skilled bimanual actions involving tools, a group of healthy individuals had to be tested with conditions including interactions with tools and non-functional objects. Such experiment was performed by Vingerhoets and collaborators (2012).

The study revealed that bimanual pantomimes of tool use strongly engage the left premotor and posterior parietal cortices when contrasted with unimanual pantomimes of skilled movements with tools, regardless of whether the participants were right- or left-handed (Vingerhoets et al., 2012). This result is in line with the notion that higher-level brain mechanisms for object manipulation can in fact be hand-independent (Kroliczak et al., 2016; Kroliczak & Frey, 2009). However, the control condition in this experiment involved pantomimed movements of eggs – one around another, and one in each hand (see Figure 1). Importantly, eggs are natural, palatable objects which have no other potential affordance than precision or power grip, moving towards mouth, and maybe throwing or smashing them. Hence, what should be considered next are control objects with similar grasp affordances to tools, but with no specific function to be performed after the grasp. Moreover, providing control with more complex kinematics of grasping and the following movements can reveal effects specific to movement coordination, which is required for a successful manipulation of bimanual tools. Finally, different functional inputs should be required for each of the hands (leading/dominant

vs. upholding/positioning hand) – this can underline the specific contributions of the right hemisphere to the additional control for a non-preferred hand and/or overall parallel guidance of both effectors.

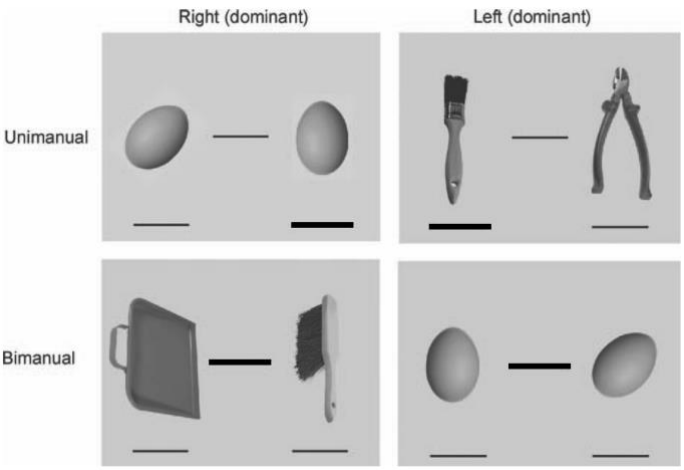

Figure 1. Experimental conditions from the study by Vingerhoets and collaborators (2012). The thicker line informed the participants that they should perform either the unimanual (with an underlined object) or bimanual pantomime of object use (when the line was between the objects). In the control condition involving eggs, participants either rotated their wrists while holding an imaginary egg (a unimanual action) or moved one imaginary egg around the other (a bimanual control condition). The Figure is adapted from Vingerhoets et al., 2012.

As Vingerhoets and colleagues were primarily interested in the execution phase of an action, they used an experimental block design. Yet, not incorporating planning phase into study design, can further weaken a limited ability the block-design has for differentiating between particular phases of the interaction with tools (see Johnson-Frey et al., 2005; also discussed further on). Moreover, as mentioned earlier, control objects, which were used in this experiment, belong to a different category than experimental stimuli (food items vs. tools), and the subtraction of signals related to food-item processing can result in a substantially different brain pattern. Another issue is the choice of control items, and the resulting lack of an appropriate linguistic control condition for numerous tools used as stimuli. In other words, there are some clear differences in both sensori-motor and linguistic processing demands, as well as other factors loosely linked to praxis processing.

One of the final weaknesses of Vingerhoets et al.'s (2012), and many other studies (e.g., Buxbaum et al., 2014; Ogawa & Imai, 2016; Ramayya et al., 2010), is the utilization of pantomimed tool use as a proxy to real tool use actions. Despite the undisputed usefulness of pantomimed actions (gestures), including gestures involving tools, in the diagnosis of apraxia (Goldenberg et al., 2003), movement kinematics involved in using imagined vs. real (actual)

objects may substantially differ (Laimgruber, Goldenberg, & Hermsdörfer, 2005; see also: Singh et al., 2019). Moreover, it has been demonstrated that using real objects in experimental paradigms can elicit faster and more accurate behavioral responses, which suggests that affordances of actual tools are significantly stronger than the ones of 2-D images of these tools (Gomez et al., 2018).

Although Vingerhoets et al. (2012) focused on the *use* (*execution*) phase of an action, recent evidence shows that the preparatory phase (planning of grasping movement) can be more important than previously thought (cf. Brandi, Wohlschlager, Sorg, & Hermsdorfer, 2014; Przybylski & Kroliczak, 2017). The evidence shows that the substantial part of higher-level processing can be performed even before the onset of an action, only for the movement to be guided motorically in real time during grasping. Meanwhile, the block design used by Vingerhoets and colleagues would not allow for the extraction of these specific, planning-related signals. Neural activity during grasp planning can be especially important, as interactions with bimanual tools are of course more complex than with unimanual ones. Although modeling the planning phase of an action is possible in the block-design paradigm (see for instance: Freud et al., 2018; Gallivan, McLean, Smith, & Culham, 2011; Gallivan, McLean, Valyear, Pettypiece, & Culham, 2011), fMRI brain volumes as long as 2000 ms are unlikely to reveal the specificity of planning-related brain activity. The general, temporal patterns of grasp planning is revealed in electroencephalography studies, such as in the study on the functional role of beta oscillations in planning and execution of grasping movements by Zaepffel and colleagues (Zaepffel et al., 2013). Given these weaknesses of a block-design paradigm, an alternative approach in fMRI is the utilization of an event-related design. In fact, modelling relatively shorter signal changes allows to introduce an additional "jitter", i.e., variable time intervals between planning and performing an action (see Poldrack, Mumford, & Thomas, 2011). This, in turn, can contribute to increasing event-related signal activity and diminishing the influence of repeatability and automatization of tool-directed actions (for such potential confounding effect, related to neural signal adaptation, see, e.g., Kroliczak et al., 2008). In order to study tool-related brain activity with an event-related design, at least three events-of-interest should/could be modelled.

1.2.4 Planning functional grasps, grasping, and using tools

Interactions with functional objects can be divided into several distinct phases, including: grasp planning (Johnson-Frey et al., 2005; Przybylski & Kroliczak, 2017; Baltaretu et al., 2019), grasping an object (Castiello, 2005; James et al., 2003), and performing tool-related actions

(Goldenberg & Spatt, 2009; Baltaretu et al., 2019). Although each of these phases was intensively studied as a separate phase of an action, there were only few attempts to model the interaction with a tool as a continuous process – from grasp planning, through grasping to using tools (see, e.g., Brandi et al., 2014; or Przybylski & Kroliczak, 2017). As a matter of fact, such continuous interactions with functional objects were not yet studied in the context of bimanual tools. Nevertheless, in order to devise an experiment on planning, grasping and using bimanual tools, each of these phases of an action has to be precisely defined.

First, it has been established that planning tool use pantomimes engages different brain mechanisms than their execution (Johnson-Frey et al., 2005). Planning tool use gestures with the right hand engages mostly the left-brain hemisphere, including: the posterior parietal cortex, posterior temporal, inferior-middle frontal cortices, and dorsolateral prefrontal cortex (DLPFC). On the other hand, executing tool use gestures invokes the neural activity within both hemispheres, with similar regions being involved as during the planning phase. Although such an activity is observed in both hemispheres, additional strong inputs from the contralateral, left hemispheric sensorimotor cortex are also revealed. Interestingly, when the same right-handed participants were tested for brain activity associated with planning and executing tool-use gestures with their non-dominant left hand, the results were generally the same for planning (left-hemispheric dominance), but the sensorimotor activity was observed in the right hemisphere now, i.e., in the brain hemisphere contralateral to the used hand.

A very precise definition of *grasping*, and *functional use* of tools, as well as non-tool objects was given by Vingerhoets (2014), with the emphasis being put on the role which the parietal cortex plays in grasping and using actions (Vingerhoets, 2014). According to this theoretical analysis, transitive movements executed towards a tool can in fact be divided into at least two phases or components: an initial *reaching* movement, and the subsequent *grasping*, i.e., the "merging of hand and object". Although I was aware of this distinction, because the primary scope of my thesis was *planning* actions towards tools, in my experiment I collapsed these two theoretically distinct components of a transitive movement towards an object, and they were jointly modelled as the *grasping* phase. Thus, further in this dissertation I will utilize the *planning-grasping-using* theoretical framework, although I am fully aware that a more fine-grained paradigm of *planning-reaching-grasping-using* is also a very interesting lead which is definitely worth studying in the future.

While going through the literature on interactions with tools, one conspicuous fact can be noticed, namely, that a *planning* phase of an action was always considered as planning *tool use* gestures. In other words, what the participants were instructed to do was: "*to plan tool use*

gestures". Noteworthily, however, Przybylski and Króliczak (2017) suggested a slightly different approach – they asked their participants to plan *functional grasps* of tools. It was shown by these authors that planning functional grasps of tools elicits changes in the left-hemispheric PRN activity. This is quite a surprising outcome, given the fact that all theories and experiments prior to this study were focused on *tool use* and *planning tool use actions*, and actually none before aimed at disentangling the *grasp* component from the *use* component of *planning* an action. Meanwhile, it turned out that by including *planning functional grasp* into an experimental paradigm, it can be demonstrated that the left hemisphere activity, commonly associated with *tool use* preparatory processes, is in fact to the greater extent responsible for planning functional grasps, not only tool use *per se*. In such a vein, it might be the case that the actual tool use is planned during grasp execution (see Raś, 2019), or even later on: while already holding a tool in hand – i.e., in real time, as the action develops. This result shows the importance of differentiating between planning functional grasp and planning tool use components of interactions with tools. One of the possible theoretical frameworks for such a distinction was already mentioned above, and it assumes dividing interactions with tools into three phases: planning functional grasps of tools, performing the grasps, and finally, using the grasped objects (tools).

It is known from studies on patients with left-hemisphere lesions that different brain regions are engaged in grasping as compared to using tools (e.g., Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2010). As demonstrated by Randerath and colleagues, lesions in the vicinity of the supramarginal gyrus contributed to worse tool use performance. On the other hand, if tool grasping ability was impaired, brain lesions were observed in the left inferior frontal gyrus and in the angular gyrus. Interestingly, based on studies with monkeys (Borra et al., 2008) and human participants (Goldenberg & Spatt, 2009), we know that frontal cortices might contribute to selecting appropriate grasping movement for functional or non-functional objects. Indeed, when there is virtually a countless number of possible motor outcomes to consider, preparing a proper set of movements towards a tool is "far from a trivial problem" (Rosenbaum et al., 1996). Noteworthy, information neither on the stimulus nor on one's physical state alone is sufficient for selecting an appropriate grasp from the plethora of possible movement options. In this situation, the "embodied" information about the internal dispositions of a cognitive agent is necessary to select an appropriate grasp, as Rosenbaum once noticed:

> "[…] *the perception of affordances (how best to grab a stick) does not just depend on the stimulus (the image of the stick) or on the actor's current*

physical state (e.g., the current state of the muscles and joints), but rather on information embodied in the actor's intentional state regarding what he or she wants to achieve."

Rosenbaum et al., 1996

If Rosenbaum's theory is true, it is very likely that somewhere in the brain, there is a neural circuit specialized in processing information about agent's intentional state regarding an action goal. The intention to grasp an object is clearly related to the selection of an appropriate grasp, especially in the case of tools, where what is actually meant by "an appropriate" grasp depends strongly on the context of the situation. E.g., for grasp-to-use actions a functional grasp has to be selected, and when the task is to pass someone a tool, a non-functional grasp may be more appropriate, so that the other person can conveniently grasp the handle. As mentioned earlier, in the "standard" situation, i.e., when an object is placed in front of the participant, it is the inferior frontal gyrus that is responsible for selecting an appropriate grasping movement. But what if there was an error in the initial grasp of an object? In fact, quite often it happens that we carelessly grasp some tool, and in order to use it properly, we have to adjust the grasp. This applies not only to neurological patients, but also to everyday practice. Can this category of amending grasping actions be also considered as "grasp selection" (selecting an appropriate grasp)? This problem comes down to the question of what the neural substrates of the mechanism responsible for selecting the best initial grasp are, i.e., what kind of grasp is required after transporting the hand through a substantial distance in the peripersonal space towards an object. A completely different issue is a situation when the object has been already grabbed with the hand, and some modification of the grasp is necessary.

1.2.5 Adjusting the grasp prior to tool use

Although, as described above, grasping functional objects was intensively studied in the past, one component of an interaction with tools was missing from the debate. Namely, almost all studies assumed that the initial grasp is to the greater extent appropriate and optimal, i.e., it allows for the immediate tool use. Meanwhile, under many circumstances (e.g., given an orientation of a tool) an appropriate functional grasp is not immediately possible. Then, grabbing an object in a less optimal way and amending its position in a hand, or putting it into the more proficient effector (hand), might be a necessary intermediate step. In other words, even for non-apraxic individuals, an initial grasp may often be less than optimal or appropriate for the immediate performance of an action. In the case of such "awkward" grasps, some further

movements are needed to correct/adjust the grasp in order to proficiently use a tool (for the definition of an "appropriate" grasp cf. Rosenbaum et al. 1990, 1996).

This problem is well recognized in robotics, where each process involving a robotic arm movement has to be explicitly designed in great detail first, then be implemented, and finally carefully tested. For instance, Dang and Allen (2013) showed that in the case of a simple grasp a better heuristic is rather to let the robot initially grasp the object inaccurately and afterwards adjust the grasp, than try to prepare the stable grasp from the beginning (Dang & Allen, 2013). The level of complexity of procedures in robotics provides an invaluable insight that manual operations which seem trivial from the point of view of human performance are in fact governed by a sophisticated mechanism shaped by tens of thousands of years of the evolution.

Nevertheless, in robotics, usually relatively simple movement sequences are considered, while when studying human intention to properly grasp a tool, grasp correction is determined primarily by the to-be-achieved goal (see, e.g., Valyear, Chapman, Gallivan, Mark, & Culham, 2011). Needless to say, the specific human brain mechanisms governing such sophisticated motor transformations for grasping and the subsequent grasp adjustment, remain largely unknown. Moreover, such adjustments may play an important role not only in unimanual interactions with tools, but also in preparing bimanual actions with tools. In fact, given the necessity to coordinate the movements of both hands, adjusting the grasp may be even more important for bimanual actions directed at tools (Swinnen, 2002).

Interestingly, a common situation in which we have to adjust our initial grasp of a tool is when this tool is being passed to us, or when we want to give a tool to somebody else. If a person passing the tool to us is holding the tool by its handle, and the functional part of a tool is directed towards us, we have to either grasp the tool at its functional part, or to grasp the tool in some other place in the handle, which is not occupied by the hand of a person who is giving us the tool. After such a non-optimal grasp, we have to adjust the grasp in order to efficiently use a tool (see, e.g.: Jax & Buxbaum, 2010; Squires, Macdonald, Culham, & Snow, 2016; Valyear, Chapman, Gallivan, Mark, & Culham, 2011). A similar case is when, for various reasons, the initial grasp needs to be performed with our non-dominant hand. Then, at least strongly right- or left-handed people most probably will have to pass such a non-optimally grasped tool to their more proficient effector. For bimanual tools the situation is even more complicated, because not only the grasp might have to be adjusted, but sometimes it may even be required to switch the handled parts of a tool (e.g., if the tool has multiple parts). Ultimately, for bimanual tools, both the dominant and supporting hands have to firmly hold a tool.

From the perspective of the neural underpinnings of grasp adjustment, the question remains whether the same higher-level parieto-frontal neural mechanisms responsible for the selection of the appropriate initial grasp are also involved in adjusting grasps later on. One of the alternatives is that this adjustment is merely a sensorimotor and proprioceptive trial-and-error procedure, most likely processed within the sensorimotor cortices and/or within the parietal cortex (Vingerhoets, 2014).

Another question is, whether skilled manual actions are processed either on higher or lower level regardless of the level of complexity of the action. Namely, even if grasp selection of simple, unimanual objects was processed exclusively in the sensorimotor cortex and intraparietal sulcus, it does not mean that the same is the case for complex bimanual tools, where additional information such as coordination has to be considered. In other words, movement selection criteria may differ, depending on the complexity of a task.

1.3 Bimanual and unimanual tools. Current project

Thus far, the theories behind actions with tools and particular phases of these actions, including planning functional grasp, have been presented. The importance of the distinction of particular stages of action: planning, grasping and using, will become even more evident when the characteristics of unimanual and bimanual tools are introduced. Although, as presented above, some aspects of bimanual actions have already been studied (Heitger et al., 2012; Vingerhoets et al., 2012), the phenomenon of movement coordination and differentiation between phases of such actions have not been considered. Hence, in order to study in-depth interactions with this very specific category of functional objects, i.e., bimanual tools, two categories of tools should be distinguished:

- Unimanual tools are simpler, one-handed functional objects, which in order to be used in a functional manner, do not require bimanual coordination. An exemplar of the unimanual tool category are one-handed rakes, for which only one effector is engaged in an action, and a set of movement trajectories to perform such an action is restricted to one hand only.
- Bimanual tools are more manually demanding objects, for which an interplay between both hands is required to perform the function of such tools. In sharp contrast to unimanual tools, intermanual coordination is the key factor for bimanual tools, and requires substantially different hand movement trajectories to perform a given activity (which can also be achieved with a corresponding unimanual tool).

Having defined the two kinds of tools, in my dissertation the notions of unimanual tools and bimanual tools will refer to functional objects (man-made artifacts) that are used to perform actions with one hand and two hands, respectively. Although it is of course possible to use unimanual tools with both hands, such a situation is not in the scope of this project. Hence, unimanual tools do not require coordinating both hands, and the action role of the hand holding a tool is clear. Bimanual tools, conversely, do involve both effectors, therefore planning and performing actions with bimanual tools involves intermanual coordination and role-differentiated bimanual manipulation. Notably, usually we do not experience a difference in increased difficulty when manipulating bimanual as compared to unimanual tools (indeed, using a new, unfamiliar unimanual tool can be more demanding than using a familiar bimanual one). Nevertheless, the subjectively perceived difficulty in using different tools is out of the topic of this thesis as well.

To sum up, tools are man-made artifacts with a designated function, which require movement sequences with one, or a coordination between two hands. Hence, in this vein, tools differ from non-functional objects such as wooden branches, sticks, stones or shells which can be also used by animals (Chappell & Kacelnik, 2002; Finn et al., 2009; van Schaik et al., 1999). According to some other definitions of tool use, non-functional objects utilized to obtain a specific goal can be also treated as tools (e.g., see a broader definition of functionality by Frey, 2007, and using tools to acquire food – van Schaik et al., 1999). Such broader understanding of tool use is irrelevant for my thesis, because here I consider tools as objects having some predefined function – focusing on object affordances – and not all possible actions with a given tool (see: Vingerhoets, 2008). For the comparison of the discussed specific categories of objects see Table 1.

Table 1. A summary of the definitions of: unimanual tools, bimanual tools, unimanual graspable non-functional objects, and bimanual graspable non-functional objects, as used in this dissertation.

	Unimanual tools	**Bimanual tools**	**Non-functional unimanual objects**	**Non-functional bimanual objects**
Extending capacity of the body	+	+	+	+
Having a predefined function	+	+	–	–
Requiring intermanual coordination	–	+	–	+
Example	screwdriver	hedge clippers	sticks, rocks	larger branches, peeling action

A primary research question in this thesis regards the neural representations of planning functional grasps of bimanual tools preceding tool use, with the hand coordination component being crucial for both functional grasp and subsequent use of tools. As it is not clear when the processing of the coordination component takes place, my research paradigm assumed distinguishing three phases of neural computations related to the target action. Specifically, after the action planning stage (preprogramming of the functional grasp movement), there was a grasping phase – where the movement toward an object took place, followed by the execution of unimanual or bimanual tool use. Planning interactions with functional objects (tools) when compared to planning interactions with non-functional objects invokes neural activity within PRN, i.e., such mental actions involve higher-order brain mechanisms. The question is, whether planning interactions with bimanual tools also involves PRN, and, if yes, what pattern of activity within this network is obtained, as compared to grasp-preparatory mechanisms for unimanual tools. Alternatively, if the coordination component of bimanual interaction with tools can be processed outside of the PRN – then my study should reveal what the crucial brain loci for preparing coordinated grasps of tools are.

Finally, studying bimanual interactions with tools exposes the problem of preparing the most appropriate initial grasp, i.e., people often need to grasp the object in a less optimal way in order to handle it more appropriately later on, after some amendments (correcting the grasp if necessary). An additional experiment I performed was to reveal the potential influence of grasp amendment/adjustment to the results obtained in the main experiment.

In the light of the above discussion, three hypotheses can be formulated:

- A corroboration hypothesis:

  (H_C) The left lateralized network comprising **cMTG**, **aIPS**, **aSMG**, **cSPL**, **PMd**, **PMv** and **rMFG** is more engaged in **planning tool use actions** – regardless of whether unimanual or bimanual – when compared to planning interactions with non-tool objects.

- The main hypothesis:

  (H_M) There are PRN nodes that are differently engaged in **planning and/or performing grasps** for bimanual tools use when contrasted with unimanual tools.

- The supporting hypothesis:

  (H_S) Grasp selection mechanisms are engaged not only in the initial grasp of bimanual tools, but also in the subsequent **grasp adjustment**.

All three hypotheses will be verified with a whole-brain analysis at the hand-independent level. Moreover, the main hypothesis (H_M) will be tested for each hand separately, utilizing a region-of-interest approach.

Chapter 2. Materials and methods

2.1 Participants

Twenty strongly right-handed (Edinburgh Handedness Inventory index: *M*=94.4, *SD*=9.6; Oldfield, 1971) participants (10 females) volunteered for this study. All of them were native Polish speaking students from Poznan Universities (age range 20 to 27; *M*=22.8; *SD*=2.1) and had normal or corrected-to-normal visual acuity. During the training preceding the scanning for at least one day, pre-scan MRI safety questionnaires and a written informed consent was obtained from each volunteer after she/he was acquainted with study premises and procedures. Following a successful study introduction, participants were presented with stimuli and practiced the required responses in a training session. After study completion, each participant was reimbursed financially for her/his time and effort, and debriefed. All study protocols and procedures were evaluated by the Bio-Ethics Committee at Poznan University of Medical Sciences, which agreed that all the utilized procedures conformed to the principles of the 2013 WMA Helsinki Declaration.

2.2 Stimuli

The stimuli used in this experimental project were real objects: twelve bimanual and twelve unimanual tools, which corresponded in such a manner that the function of each stimulus pair was matched, e.g., unimanual kitchen knife and bimanual herb knife. (For a similar approach to functional equivalence in the case of unimanual tools differentiated by sensori-motor constraints, see Cardinali et al., 2016.) All tools were plastic or wooden and, therefore, these objects could be used within the scanner room without disturbing the magnetic field or being pulled into the scanner (thus posing a danger to a participant). Additionally, there were two wooden control objects, namely, a single prolonged solid cylinder for unimanual grasps, or two parallelly attached cylinders for bimanual grasps.

All stimuli were placed in the middle of the platform, a part of the simplified *Grasparatus* used elsewhere (see Nowik et al., 2019; Styrkowiec et al., 2019). The position of the objects remained the same, regardless of whether the right, left (for unimanual objects), or both hands (for bimanual objects) were used. There were two exceptions from that rule, however: a *hammer* and *chisel*, as well as a *sweeper* and *dustpan*. These two pairs of objects were placed correspondingly to the to-be-used (leading) hand, i.e., if the task was to plan the functional grasp with the right hand the *hammer* was put on the right, while *chisel* on the left, and *vice*

versa if a participant was using the left hand. The same rule applied, correspondingly, to the *sweeper* and *dustpan*.

The bimanual tools could be further divided according to three criteria: (1) the *hammer* and *chisel*, and *sweeper* and *dustpan vs*. the remaining objects (for the reason explained above); (2) if the tool was used in the same manner regardless of the *leading* hand: *herb knife*, *rolling pin* and (in some sense) *hedge clippers* vs. the rest; (3) if the object can be detached (a tool consists of two separate objects): the *hammer* and *chisel*, *sweeper* and *dustpan*, *nutcracker*, *mortar*, *squeezer* and *twist lid container* vs. *the remaining objects*.

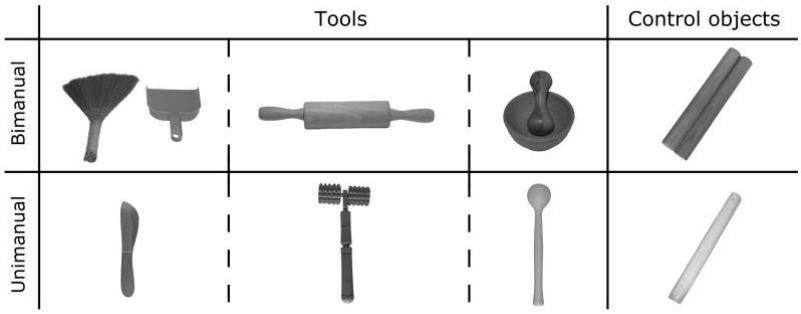

Figure 2. Stimulus examples. Bimanual and unimanual objects (both tools and control objects) used in the experiment. The three columns for bimanual tools correspond to the three classes of objects described in section 2.2., namely: (1) interchangeable between hands at the moment of functional grasp planning (upper leftmost cell), (2) used symmetrically (upper middle), and (3) detachable objects (upper rightmost cell for tools). The complete list of stimuli can be found in Appendix A.

Additionally, in my experiment, the stimuli were real objects, as the primary interest was to emulate real-life experience with objects (Berti & Frassinetti, 1996; Culham et al., 2006). In other words, this manipulation would provide a better "ecology" of the studied phenomena (Gibson, 1979). Of almost equal significance was the task paradigm, hence an event-related design (instead of blocks of trials) was utilized in the current experiment. This allows to disentangle the contribution of the preparatory (planning), the grasping phase, as well as the subsequent execution of tool-use action (as in Kroliczak & Frey, 2009, and Przybylski & Kroliczak, 2017; see also Buchwald, Przybylski, & Króliczak, 2018).

2.3 Data acquisition

The data were obtained with a Siemens Magnetom Spectra 3T MRI scanner at the *Rehasport Clinic* in Poznań, Poland, with a 16-channel radiofrequency transmission and reception coil. A T2*-weighted gradient echo sequence was used to acquire echoplanar images (EPIs) with time to repetition (TR) = 2000 ms; time to echo (TE) = 30 ms; flip angle (FA) = 90°; 64 × 64

voxels matrix; field of view (FOV) = 200 mm; 35 contiguous axial slices, 3.1 mm isotropic voxels (in-plane resolution of 3.125 × 3.125 mm, and slice thickness of 3.1 mm). Each run of the main experiment comprised of 277 functional volumes, and in the additional experiment there were 185 volumes. The experimental design of both the main and additional experiment are described in the following sections (starting from 2.4).

High-resolution, T1-weighted structural images were obtained with magnetization prepared rapid gradient echo (MP-RAGE) pulse sequence: TR = 2300 ms; TE = 3.33; inversion time (TI) = 900 ms; FA = 9°; 240 × 256 matrix size; FOV = 240 × 256 mm; 176 contiguous axial slices; and 1.0 mm isotropic voxels. Additionally, a fast spin echo T2-weighted structural image was acquired (TR = 3200 ms; TE = 402 ms; FA = 120°; 512 × 512 voxel matrix size; FOV = 256 mm; 192 contiguous sagittal slices; with 1.0 mm isotropic voxels), to improve registration of the functional scans to the T1 structural image. The raw DICOM data obtained with the scanner were subsequently converted to NIfTI-1 format using MRI-Convert software[2].

2.4 Task paradigm

In this section experimental procedures will be presented. First, I will describe the paradigm of the event-related main experiment, and then I will describe additional tasks from the block design experiment. The latter always took place after the main experimental runs. Notably, virtually the same stimuli were used in both experiments, with the restriction that in the additional experiment the control objects were not used, and the objects that are typically used in the same manner, regardless of the *leading* hand (see point '(2)' of paragraph *2.2.*), were also excluded. The experimental setup, the researcher running the study, and a study participant are shown in Figure 3 below.

[2] MRI-Convert can be obtained at: http://lcni.uoregon.edu/downloads/mriconvert

Figure 3. Experimental setup. A participant is laying supine in the scanner. The stimuli are presented on a magnet-friendly platform, a part of the *Grasparatus* device (no ferromagnetic materials; see Nowik et al., 2019) with the size matched to the width of the scanner's bed on which the participant is lying. The picture was taken during the main experimental run; the head coil mirror allows the participant to see the table with the stimuli on it. The experimenter is monitoring task performance by the participant.

2.4.1 Experiment 1 – Main project

On the onset of each experimental session, participants were asked to put their hands on the response pads placed on their hips, with their index fingers pushing the "start" buttons. Participants' arms were restricted with a rubber band (placed around their chests and arms) at the height of the biceps, which reminded them about avoiding to perform exaggerated movements with their shoulders and upper arms. Additional cushions were placed beneath their elbows so that they would not need to keep lifting their arms up (towards the platform) for the whole duration of each run and the whole session (~10-minute runs, 1.5-hour session). Other than that, hand and forearm movements were unrestricted.

An experimental trial was initiated with a dropping tone indicating to the participants to close their eyes, as instructed during the training sessions. Then, the stimuli were placed within the participant's reach on the previously mentioned scanner-compatible plastic platform (see Section 2.2 and Figure 3). Subsequently, a volunteer heard a rising tone (a cue for opening the eyes), saw the object(s), and heard the "*plan*" instruction, upon which he/she began planning how to perform the appropriate grasp for 3.5, 4.5, or 5.5 s, depending on the pseudo-random order (with the hands still on the control pads). Subsequently, the "*grasp*" command was issued auditorily and a participant had 3.0, 3.5 or 4.0 s to move his/her hands from the pads towards the object, in order to perform an appropriate grasp. The variable intervals for the *planning* and *grasping* phases were introduced in order to diminish the effect of getting by the participants

into the routine and performing actions “mechanically”. Finally, after receiving the “*use*” cue, he/she was supposed either to execute the sequence of movements associated with the tool, or to move the control object from one place to another. After 4.5 s the “*put down*” command was issued, and there was 5.25, 5.75 or 6.25 s left for the participant to put the object back on the table and push the start buttons on the control pads. A schematic of a single trial is shown in Figure 4. A variable time interval at trial conclusion played a role of an inter-trial interval (ITI), after which either another trial or a 12-second *rest* period occurred. (The rest intervals are not shown in Fig. 4.) Participants were told that during the *rest* periods they should try to think of nothing in particular, just lay with their eyes opened, and try not to look around too much.

In total, each participant, during a single functional run, interacted with 6 bimanual tools, 6 unimanual tools, 3 times with the bimanual control object, and yet another 3 times with unimanual control stimuli. That gives 12 experimental and 6 control trials in each run. These conditions were intermixed with 6 rest periods for the signal to return to baseline, which at the same time gives a basic reference condition (e.g., for ROI signal percent change analyses). The presented stimuli were pseudo-randomly organized into 5 runs. (An additional training run was performed during preliminary training away from the scanner environment, usually on the day preceding the first scanning session.) The presented numbers of trials and runs, for the 20 participants, give in total: 6*5*20=600 bimanual trials (*number of experimental trials per run * number of runs * number of participants*), 6*5*20=600 unimanual trials, 3*5*20=300 control bimanual trials, 3*5*20=300 control unimanual trials (*number of control trials per run * number of runs * number of participants*), and 6*5*20=600 resting intervals (6 rest periods per run). In sum, there were 1200 experimental trials, 600 control trials and 600 rest intervals. All conditions were intermixed in a pseudo-random order. The orders of trials are available in the Appendix C of this thesis.

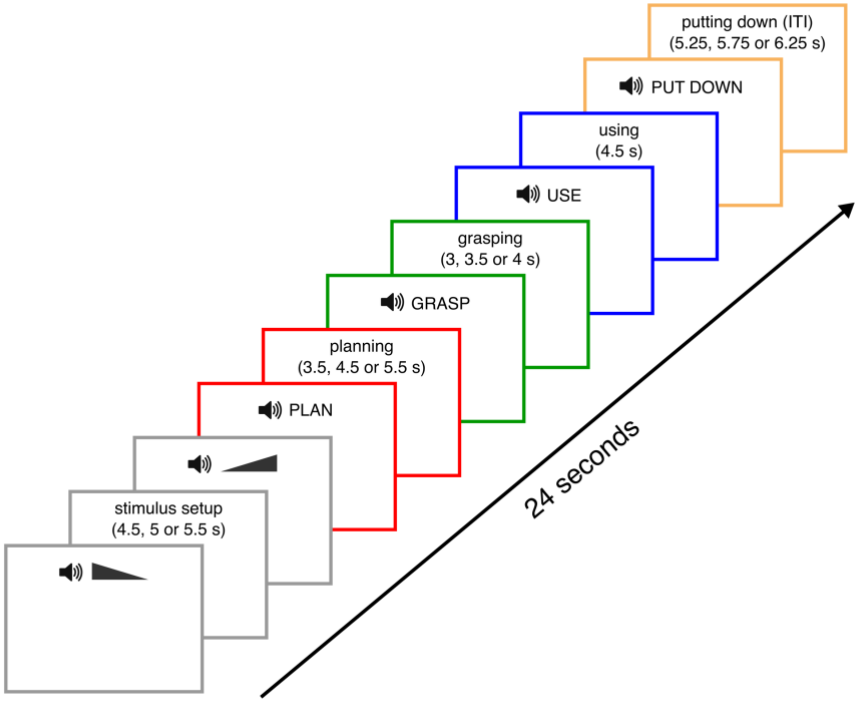

Figure 4. Trial structure and timing utilized in the paradigm of the main experiment. First, there was a dropping tone indicating to the participants to close their eyes. At that time (a variable 4.5, 5.0 or 5.5 s interval) a stimulus was prepared on the table. Following the subsequent rising tone (a cue to open the eyes) and the auditory cue ("PLAN"), participants were planning a functional or control grasp of an object (for 3.5, 4.5 or 5.5 seconds in total, as marked by red frames in the figure). Similarly, during the grasping phase (initiated with the auditory "GRASP" command), they grasped and handled (but not yet used) the object. Finally, following the auditory "USE" cue participants were either using a tool in a functional manner or they were transporting the control object from one place to another (i.e., displacing them, cf. Vingerhoets, Acke, Vandemaele, & Achten, 2009). After a trial, the object was put down and participants were waiting (for 5.25, 5.75, or 6.25 s) for the following commands or for the rest intervals.

My rationale was as follows: the to-be-used hand (or the "leading" hand in the case of bimanual objects), the effector used (unimanual or bimanual action) and object functionality (tool or control object) may jointly differentiate blood oxygen-level dependent (BOLD) signal response during adequate grasp planning. By *adequate* I mean functional grasp in the case of tools and performance of corresponding movements in case of control objects. The most important comparison in my analyses would be the difference between the following two contrasts: (1) *planning functional grasp of unimanual tools* (pUT) vs. *unimanual control objects* (pUc) and (2) *planning functional grasps of bimanual tools* (pBT) vs. *bimanual control objects* (pBc). If statistically significant differences between these two subtraction results were obtained (i.e., [pBT > pBc] > [pUT > pUc]), it would mean that an object's "*manuality*" (i.e., whether it is bi- or unimanual) cannot be marginalized. Alternatively, this question could be formulated as the

differences: first, *between* the number of effectors (hands) required to manipulate the object (bi- vs unimanual), and then *between* the object type (its *functionality*, i.e., tools vs. non-tools); schematically: [pBT > pUT] > [pBc > pUc].

The vast majority of previous studies implicitly generalized the results obtained with unimanual tools to all tools (i.e., putatively extended their outcomes to bimanual tools), which may not be totally legitimate in the case of planning functional grasps of tools, grasping them and finally using these objects (a clear separation of particular task phases was used, e.g., in works by Gallivan and collaborators, 2011, and Chen and colleagues, 2019). Although there is some evidence that the results of performing grasps of handles of a stationary device may be generalized from uni- to bimanual manipulation (Freitas et al., 2007), such a definite report in the case of tools themselves is lacking. Thus, in my experiment I used real functional objects (tools) in order to provide such evidence for each of the stages of interaction with the tool separately: *planning*, *grasping*, and *using the tool*. To increase the explanatory power of the to be performed tests, participants were asked to plan functional grasps, execute these preplanned grasps, and use the tool according to its function with either of the hands being the *leading* hand, as opposed to the other being more *supportive*. For unimanual tools these actions were completed with either the dominant (right) or non-dominant (left) hand; for bimanual tools, one of the hands had a more active role, and the other was more for supporting the bimanual tasks. While tool-related skills are primarily lateralized to the left hemisphere (within PRN), independently of the hand used to perform the task (see the evidence from GLM subtraction contrasts: Kroliczak & Frey, 2009; Przybylski & Kroliczak, 2017; and MVPA: Buchwald et al., 2018; Ogawa & Imai, 2016), the inclusion of all of these three factors (*hand*, *task*, *tool-type*) enables corroboration (or confrontation) of results obtained in previous experiments and examination whether there are any substantial differences within PRN. If the interplay of these factors turned out to be significant, this could add up to what is known about the praxis skills being necessary for planning interactions with and successfully performing actions on tools.

2.4.2 Experiment 2 – Additional experiment

Participants stayed in the scanner in exactly the same position as during the main experiment. They were asked to grasp tools that were handed over to them by the experimenter [MB], to adjust the grasp if needed, and to perform the action with a given tool. This additional experiment comprised of 5 conditions: (1) adjusting grasps of bimanual tools and performing an action; (2) performing an action immediately after grasping bimanual tools, i.e., control for condition ‘(1)’; (3) adjusting grasps and performing an action for unimanual tools;

(4) performing an action immediately after grasping unimanual tools – control for condition '(3)'; and (5) rest intervals.

A *convenient* grasp afforded an immediate performance of an action associated with a tool, and, conversely, an *inconvenient* grasp required adjusting the grasp first. To be more specific, for an inconvenient grasp, unimanual tools had to be passed from the *non-leading* hand to the *leading* hand. Correspondingly, in the case of bimanual tools, movements with both hands had to be coordinated to switch the object or its parts so that the tool could be used in a *convenient* way. In half of the trials for both conditions, the dominant (right) hand was the leading one, and for the other half it was a non-dominant hand (left) that was the leading one. E.g., if there were 8 blocks of condition involving adjustments of the grasp of bimanual tools and performing an action, then half of them (4) was performed with the right hand being the leading one, and the other half (also 4) with the left hand playing an active leading role, depending on the day the scanning took place. For the visualization of the design of this experiment see Figure 5.

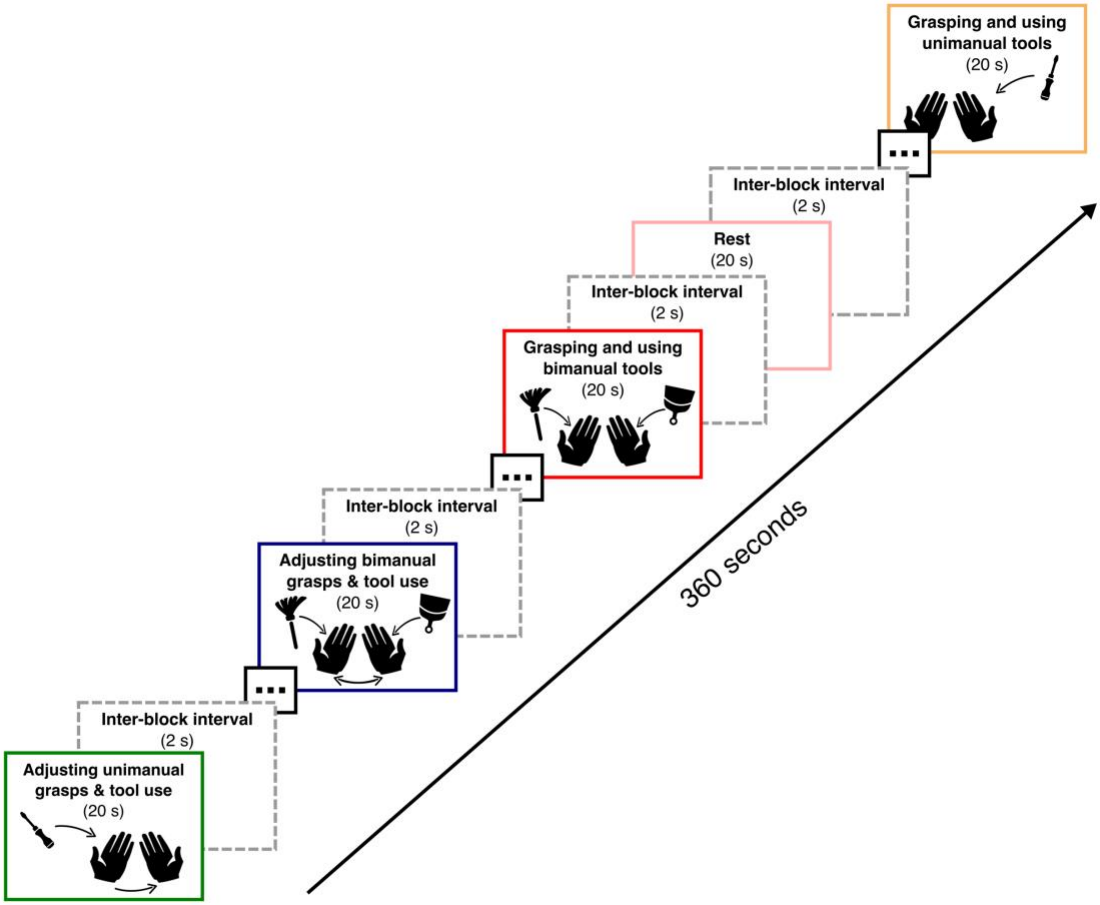

Figure 5. Run structure and timing utilized in the paradigm of the additional experiment. Conditions in this experiment were organized in 20-s blocks, separated by 2-s inter-block intervals. There were five conditions in this experiment: (1) adjusting grasps of bimanual tools and performing a tool use action; (2) performing a tool use action immediately after grasping bimanual tools, i.e., a bimanual control condition for '(1)'; (3) adjusting grasps and performing a tool use action for unimanual tools; (4) performing a tool use action immediately after grasping unimanual tools – a unimanual control condition for '(3)'; and (5) rest intervals. Within each block there were four 5-s tool-related events, i.e., participants interacted with four tools, one by one. In the example graphics depicting actions with tools in this figure, the right hand is the leading one but the number of experimental runs with right hand leading and left hand leading was equal. Within the same experimental run, one of the hands was always a leading one.

The dropping sound was the que for the participant to prepare for the grasp of the first stimulus in a given block (with the eyes always open), and subsequently this same dropping sound indicated when to stop performing the action with the current tool. This way the experimenter could switch the object in a participant's hand(s) for another stimulus, or just to take the object, if that was the last object within a given block (see Figure 5). In a single experimental block, there were four 5-s tool actions to be performed, one after another.

Data from one run of an additional experiment in the first participant were lost due to malfunction of the synchronization of the scanner and/or computer controlling the experiment. The cause of the malfunction was detected, corrected, and the subsequent 39 sessions concluded without interruptions (i.e., there were 20 participants × 2 hands each = 40 sessions, minus the one session with one of the hands from the first participant).

2.5 Data analyses

2.5.1 Data preprocessing

Anatomical T1- and T2-weighted scans were preprocessed with FSL (FMRIB's Software Library[3]) v5.0.9 (Jenkinson et al., 2012). In detail: images were first reoriented and cropped to the skull itself; FSL's brain extraction tool (BET) was used to strip off non-brain structures from the scans; and subsequently, two MP-RAGE (T1-weighted) images obtained for each participant (one per session) were spatially averaged using FLIRT (FMRIB Linear Image Registration Tool). $T2^*$-weighted scans (containing bold signal) were also preprocessed with a default BET tool, and were motion-corrected with FSL's algorithm (with FLIRT). Spatial smoothing of 6.2 mm (twice the voxel size) was performed with full-width-half-maximum (FWHM) Gaussian kernel, in addition to high-pass filtering of $\sigma = 50.0$ s.

2.5.2 Whole-brain GLM subtraction

At the first stage of the fMRI data analysis, general linear model contrasts were calculated for each run separately. Pre-whitening procedure was also applied in order to make the statistics valid and maximally efficient[4] (see Woolrich, Ripley, Brady, & Smith, 2001). Double-gamma canonical function was used to model hemodynamic responses of the brain. The planning phase was defined as the 3.5-s interval from the onset of the "planning" que (the auditory command); while the remaining 1.0 s (summing up to 4.5 s) or 2.0 s (5.5 s) delay intervals were not modelled here. The assumption behind this approach was such that the planning of functional grasps would not last for a prolonged period of time. At the second level of the analyses, individual runs were averaged. Group (third-level) analyses were performed with random-effects components of mixed-effects variance using FSL's FLAME 1 algorithm (Beckmann et

[3] FSL wiki: http://fsl.fmrib.ox.ac.uk/fsl/fslwiki

[4] See the excerpt from fMRIB's technical report on the FILM - Voxelwise Timeseries Analysis: https://www.fmrib.ox.ac.uk/datasets/techrep/tr04ss2/tr04ss2/node3.html#fig:eff

al., 2003). The obtained *Z*-scores (Gaussianized t/F statistics) were thresholded by setting FEAT's parameter to $Z > 3.1$, $p = 0.001$, followed by corrections for multiple comparisons (cluster-wise adjustment) applied at $p = 0.05$ significance level.

2.5.3 Main effects and interactions

The question I asked in my work was if praxis theory accounts for the *manuality* of tools, i.e., whether the interactions with unimanual and bimanual objects differ in terms of their neural underpinnings. More specifically, the question is whether or not divergent brain mechanisms can be distinguished for processing functional grasp preparatory mechanisms for unimanual tools (known to be processed in the left-lateralized praxis representation network), as opposed to bimanual tools, which require coordinated movements of two hands. In order to answer this question, I could not simply perform the direct comparison between bimanual and unimanual tools because the differences could arise due to divergent kinematics, and vast visual discrepancies between these two categories of functional objects. Thus, a more appropriate comparison requires a subtraction of a control condition, to account for the two just mentioned potential confounding factors. The straightforward approach to address this research question is, therefore, to utilize the following 2×2 factorial design, with factors: *manuality [levels: (A) bi- and (B) unimanual objects]* × *functionality [levels: (A) tool and (B) control object]*. If there is any interaction between these two conditions then the praxis theory would have to account for the *manuality* of a tool, e.g., by providing additional assumptions for the difference between unimanual and bimanual objects within theory's predictions. Otherwise, the theory would not have to be extended by such assumptions, as predictions related to the neural underpinnings of bimanual tool actions could be explained in terms of their unimanual counterparts, or more generally – as both categories being just tools.

However, the 2×2 design described above assumes that the *hand* factor is balanced across subjects and plays no role in how the signal is processed during planning bimanual grasps of tools. Yet, as the influence of the hand factor was *de facto* not extensively studied before with real tools, I decided to include this factor in my design, as well. Hence, the resulting analyses followed a 2×2×2 – *hand* × *manuality* × *functionality* – design.

In the main scope of my work are grasp-preparatory mechanisms, as described and explained in terms of the praxis theory. This specific phase of interacting with tools (before the onset of the grasp itself) can be studied by separating the *planning* phase of the movement towards the tool from other activities, mental or physical, associated with tools. The planning stage was represented by the first *phase* in my experimental paradigm. The following two stages

of actions with tools were: *grasping* and *using* tools. Hence, I performed three separate whole-brain rmANOVAs for each of these phases: (1) the planning phase; (2) grasping phase; and (3) using phase of an action. For even more sophisticated analysis comparing such phases directly within one test see section about ROI analysis below.

To sum up, the goal of the whole-brain rmANOVA – performed for each phase separately – was to disentangle neural representations of interactions with bimanual tools, across the cerebral cortex. This can provide a comprehensive quantitative means of understanding the nature of our interactions with bimanual tools – as compared to unimanual tools, while controlling for lower-level kinematics and visual processing of bimanual and unimanual non-tool objects.

It was obtained by setting up a specific design in FSL's FEAT[5], by which the presence of simple main effects as well as interactions could be tested. In contrast to the to-be-described ROI analyses, where all task phases are taken into account altogether, here planning, grasping and executing movements were assigned into separate models[6], as I was most interested in the planning phase. Notably, between-phase comparisons are to some extent demonstrated by the later ROI analysis itself.

2.5.4 Two disparate whole-brain repeated-measures ANOVAs were utilized

In the previously described analyses, input files for the rmANOVAs were contrasts of the particular subjects' brain activity from all the studied experimental conditions vs. rest intervals (or resting baseline, i.e., the longest, 14-s intervals between trials). A different approach is, however, also possible.

Therefore, I performed yet another rmANOVA utilizing contrasts of *tools* vs *non-tool control objects* as inputs. This analysis, referring to the control condition, was supposed to be conceptually equivalent to the effects studied in the works by Vingerhoets et al. (2012) and Heitger et al. (2012). It is of note that, similarly to a previous approach assigning different *phase* conditions to separate analyses, two factors in this analysis were the same as in the case of the

[5] For details on how to perform a rmANOVA in FSL the reader is referred to: https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/GLM

[6] Although it is feasible to perform whole-brain rmANOVA, even for 3 levels of a particular factor with FEAT software (e.g., factor *phase* in this particular case) – one would need to use dummy coding ("dummy variables") in order to achieve the required design. I finally decided to run separate rmANOVA analyses for each phase, as the main scope of this thesis is planning actions with bimanual tools, and in this case the results of separate analyses are easier to interpret. If one wishes to study signal fluctuations across all three phases: planning, grasping, and using bimanual vs. unimanual tools, I also performed an ROI analysis mentioned above.

previous procedure: (1) the to-be-used – leading – hand (right, left); and (2) manuality (bimanual, unimanual). Therefore, this analysis utilized a 2×2 design.

2.5.5 Region of interest (ROI) analyses

ROI analyses were performed based on 6 brain structures engaged in functional grasp planning: (1) the caudal middle temporal gyrus (cMTG); (2) anterior supramarginal gyrus (aSMG); (3) caudal superior parietal lobule (cSPL); (4) ventral premotor cortex (PMv); (5) dorsal premotor cortex (PMd); and (6) rostral middle frontal gyrus (rMFG). The selection of these functional ROIs was based on the outcomes by Przybylski and Kroliczak (2017), where voxels of peak activity within these regions were identified separately for planning functional grasps with the right (dominant) or left (non-dominant) hand – hence, there were twelve ROIs in total.

In the current study, functional ROIs defined for the right hand – center coordinates from Przybylski and Króliczak (2017) – were utilized for extracting percent signal change for the right-hand condition in my experiment (and vice-versa for the left hand). Around these spatial locations, spherical ROIs of 5-mm radius were created. Average percent signal changes within these regions were obtained with the FSL FEATQuery tool, where the input images for the analysis came from contrasts: experimental condition vs. baseline (rest intervals).

In order to account for the influence of the *phase* of the task on percent change in the BOLD signal, a 2×2×2×3 repeated-measures ANOVA was performed comprising of four factors: (1) the *to-be-used – the leading – hand* (right, left); (2) *object type* (unimanual, bimanual); (3) *object functionality* (tool, control); and finally, (4) *phase* (plan, grasp, execution). This model can account for the spatial distribution of the signal variability within the cerebral cortex that accompanies interactions with tools vs. non-tools – as the task progresses from *planning* trough *grasping* until finally *using* a tool. This ROI rmANOVA was followed by the post-hoc (pairwise comparisons) procedure, with Bonferroni correction applied.

However, there was a possibility that baseline condition (resting time periods) is not a sufficient ground truth for percent signal change. Therefore, in order to assure revealing bimanual-tool specific effect, another rmANOVA was performed, this time with control objects being a reference for signal variability. A 2×2×3 rmANOVA was then performed, with the following three factors: (1) the *to-be-used – the leading – hand* (right, left); (2) *object type* (unimanual, bimanual); and (3) *phase* (plan, grasp, execution). Note that as compared to the previous rmANOVA, object functionality was not a factor this time, as the control conditions were included in the analysis as a reference for experimental conditions. This analysis is more

conservative, than the one having rest as baseline, because signal changes between tool and control object are expected to be more subtle than the difference between interacting with tools and laying still and resting. Again, a Bonferroni-corrected pairwise comparison was performed as a post-hoc procedure.

2.5.6 Previous approaches to studying bimanuality (conjunctions and interactions)

As mentioned in the introduction, although several attempts were made to study bimanual manipulation actions, up to date, in only two of these studies neuroimaging methods were utilized: Heitger et al., 2012 and Vingerhoets et al., 2012 (in both cases it was fMRI). In the main scope of my dissertation there are mechanisms responsible for planning functional grasps, hence, due to the reasons explained above, I could not directly adapt an experimental paradigm neither from Heitger et al. (2012) nor from Vingerhoets et al. (2012). Nevertheless, while preparing my study I decided to perform a thorough analysis of the experimental designs and analytical methods used by both: Heitger, and Vingerhoets. The reason for that was that my methods could resemble as closely as possible the approaches from the two studies, thus maximizing the chance that the outcomes of my experiment could contribute to the results obtained by the other authors.

2.5.6.1 "Interaction" analysis – Heitger et al. (2012)

This is what Heitger and collaborators wrote when describing the most crucial comparison in their study:

> "*To examine interaction effects between the bimanual and unimanual observations, we first calculated the interaction contrasts* ***[(action 1 – control 1) – (action 2 – control 2)]*** *for each subject, where action 1 is the bimanual action condition (Bi) and action 2 one of the unimanual action condition (UniR or UniL), or the reverse.*"
>
> Heitger et al., 2012

The goal of this analysis was to reveal a bimanual-specific effect which could not be attributed to lower-level visual motion processing. Although this interaction yielded no statistically

significant effect in their study (Heitger et al., 2012), the idea of accounting for both unimanual conditions in a single analysis was, of course, worth noticing and including in my analyses[7].

2.5.6.2 Conjunction analysis – Vingerhoets et al. (2012)

Conceptually, conjunction or cognitive conjunction is a combination of several (two or more) subtraction outcomes (Friston, 2004; Price & Friston, 1997). It should be noted that for the sake of comparability and reproducibility I made an attempt to perform conjunction analyses as close as possible to the two key studies on the subject of bimanual manipulation in the field of neuroscience, i.e.: Heitger et al., 2012; and Vingerhoets et al., 2012. It was not an easy task, given the differences in notations used to describe statistical procedures performed with three leading software packages for analyzing neuroimaging data: FSL, SPM, and BrainVoyager. Authors using these diverse programs denote contrasts and conjunctions differently, which may be subject to criticism on the grounds of intersubjective communication and reproducibility (Miłkowski et al., 2018; Nosek et al., 2015; Poldrack, 2019).

Vingerhoets and colleagues used the following notation to describe how they compared pantomiming bimanual and unimanual actions:

> "*When bimanual and unimanual tool pantomiming are compared directly—in each case correcting for single differences between their respective control tasks: (BiToolRight*[8] *> UniToolRight) ∩ (BiToolRight > BiControlRight) ∩ (UniToolRight > UniControlRight)—it becomes clear that bimanual tool pantomimes result in additional activation in premotor/ precentral regions (L > R), the posterior parietal cortex (L ⩾ R), and temporo-occipital regions (R > L) (Fig. 2C₁ and upper part of Table I).*" [9]
>
> Vingerhoets et al., 2012

Informally speaking, in the set theory the intersection character "∩" ("*intersection*") represents an overlap of two sets, e.g., an intersection of set A and set B (A ∩ B). To be more specific, "A ∩ B" stands for a set, in which each element of the set A is also an element of the set B – these

[7] How to perform interaction analysis with FSL FEAT is explained at: https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/GLM#ANOVA:_2-factors_2-levels_.282-way_between-subjects_ANOVA.29

[8] "Right" in this context means that the pantomime was performed with the right hand in the case of unimanual objects and/or that the right hand was dominant when performing bimanual pantomime.

[9] There is an ambiguity in the quoted paragraph concerning "greater than" and "greater than or equal". "Greater than" character (">") denotes the performed contrast (e.g., "*BiToolRight > UniToolRight*"), and the "greater than or equal" character ("⩾") means that activations were much greater in one hemisphere than in the other (e.g., "*L ⩾ R*" means that the activity in the left hemisphere was greater than in the right hemisphere).

common elements fall into an *intersection* of these two sets. Now, there are two possible interpretations of what this symbol can represent in the context of fMRI analysis: (1) it is simply an overlap between voxels above some threshold (voxels significant at some z-threshold); and (2) it is a kind of a conjunctive "average" of these two, or more, contrasts performed voxelwise. The first approach, even though quite conservative, did not reveal any statistics behind the effect, but a binary mask of voxels that were active in each contrast. Meanwhile Vingerhoets et al. (2012) clearly presented statistical parametric map on the visualization. According to the BrainVoyager documentation (the program the authors used to analyze their data) this program allows performing *conjunction analyses*[10], even though it is not necessarily identical to what other softwares, e.g., SPM and FSL, do. Nevertheless, the *conjunction* described in BrainVoyager's documentation is in fact denoted with the logical conjunction symbol ("∧", which usually denotes Boolean's "AND" logical operator). In fact, searching for reports from studies in which BrainVoyager was utilized for statistical analyses shows that it is quite common to use the intersection symbol (∩) to denote conjunction analysis (see for example: Budell, Kunz, Jackson, & Rainville, 2015; Kaiser et al., 2010). Furthermore, the documentation helps to realize what the conjunction analysis really is – it is a function taking the smallest *t*-value from the contrasts that are subject to these analyses[11]:

$$t_{c_1 \wedge c_2} = \min(t_{c_1}, t_{c_2}) \tag{1}$$

where:

t is a *t*-test score, resulting from contrasting two conditions[12]

c_1 stands for the 1st compared contrast

c_2 denotes the 2nd compared contrast

Actually, the above formula may be generalized as:

$$t_{c_1 \wedge c_2 \wedge \ldots \wedge c_n} = \min(t_{c_1}, t_{c_2}, \ldots, t_{c_n}) \tag{2}$$

---

[10] See this link: https://download.brainvoyager.com/bv/doc/UsersGuide/StatisticalAnalysis/TheGeneralLinearModel.html, section "Conjunction analysis".

[11] Also lecture of the BrainVoyager forum assures us that the conjunction analysis performed with this software is not a simple Boolean AND operation (http://www.brainvoyager.com/ubb/Forum4/HTML/000385.html), but rather a statistical procedure on the pre-computed GLM results.

[12] See https://users.fmrib.ox.ac.uk/~stuart/thesis/chapter_6/section6_3.html, section *6.3.1 Subtraction Techniques*

In short, given that the conjunction test as performed by BrainVoyager is rather liberal, I decided to perform a conjunction analysis as described in the article by Nichols and collaborators (Nichols et al., 2005), using FSL software[13]. The contrasts that were fed into conjunction analysis in my experiment are matched with those from the original study by Vingerhoets and colleagues: (BiToolRight > UniToolRight) ∩ (BiToolRight > BiControlRight) ∩ (UniToolRight > UniControlRight). As the primary scope of this thesis is planning actions, the contrasts were taken only from the planning phase. Additionally, I also performed a separate analysis, restricted only to contrasts in which at least one bimanual condition was included, i.e., (BiToolRight > UniToolRight) ∩ (BiToolRight > BiControlRight). The goal of this additional conjunction analysis was to reveal bimanual-specific brain networks. Although as one may notice, it is possible to run also more general analyses, e.g., at the hand-independent level (i.e., including results for both hands into the contrasts), or to perform such analysis exclusively for the non-dominant left hand, my analyses were confined only to the right hand. This way they replicate as closely as possible the conjunction described in the work by Vingerhoets et al. (2012).

2.5.7 Visualizations

The results from the whole-brain rmANOVA contrasts were mapped to brain surfaces using the Connectome Workbench software[14] (Marcus et al., 2011). A multi-modal parcellation borders used to localize the results to specific brain areas are labelled in Figure 6 and Figure 7 (for details see Glasser et al., 2016).

[13] The author made the FSL script available at his web page: https://warwick.ac.uk/fac/sci/statistics/staff/academic-research/nichols/scripts/fsl/. I used the same script with slight modification to be also able to get the minimum of three Z-statistic images.

[14] Web page of the Connectome Workbench: https://www.humanconnectome.org/software/connectome-workbench

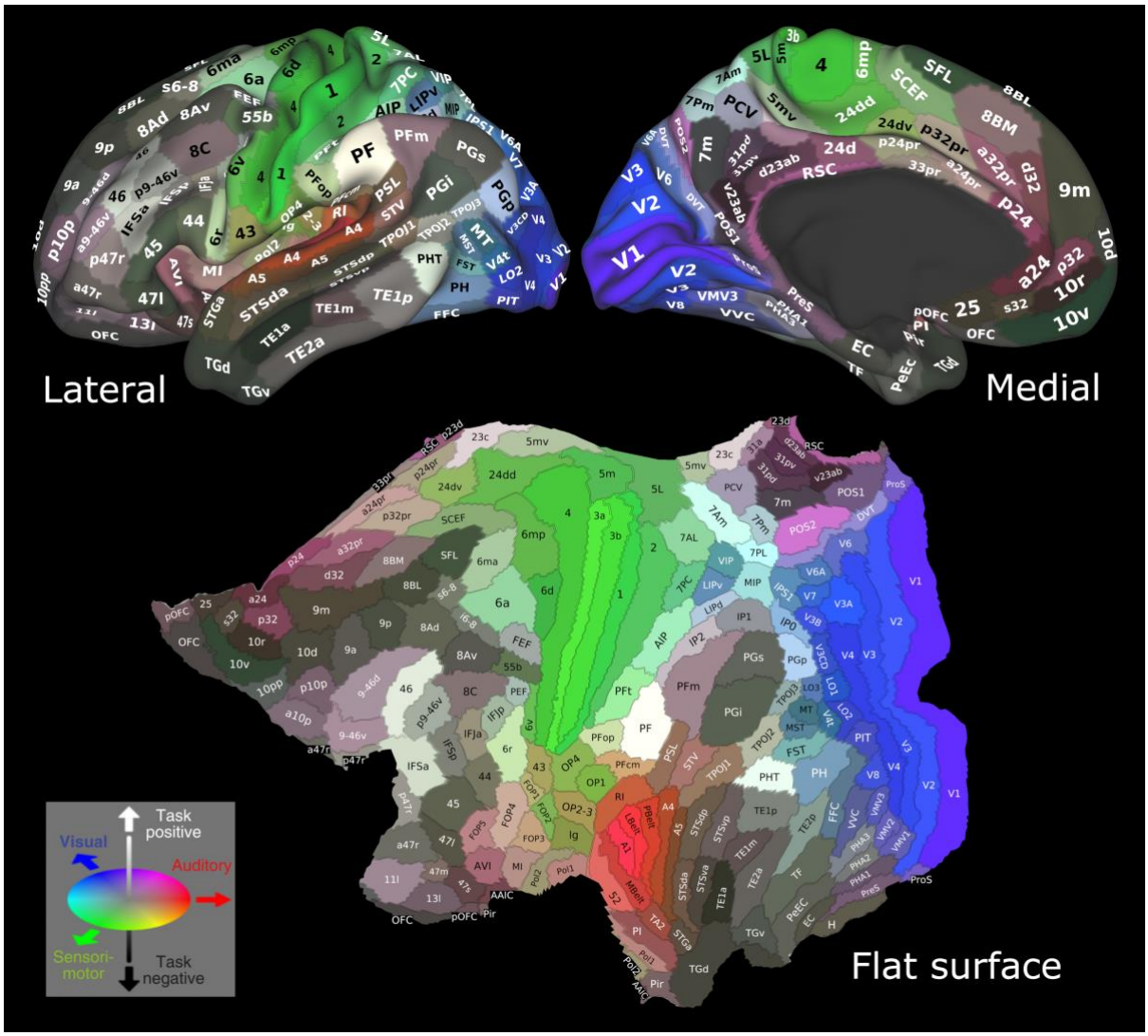

Figure 6. Parcellations of the left cerebral hemisphere. Parcellation of 180 anatomical brain areas by Glasser and collaborators (2016) mapped to partially inflated (midthickness, lateral and medial views) and flat brain surfaces for the left hemisphere. The diagram at the left bottom corner of the figure indicates the meaning of the underlying region/area color codes – modality in the horizontal plane and task-dependence in vertical direction. The complete list and the origin of abbreviations of brain areas are available in the 3rd supplementary file to Glasser et al., 2016 (*Supplementary neuroanatomical results*, Table 1).

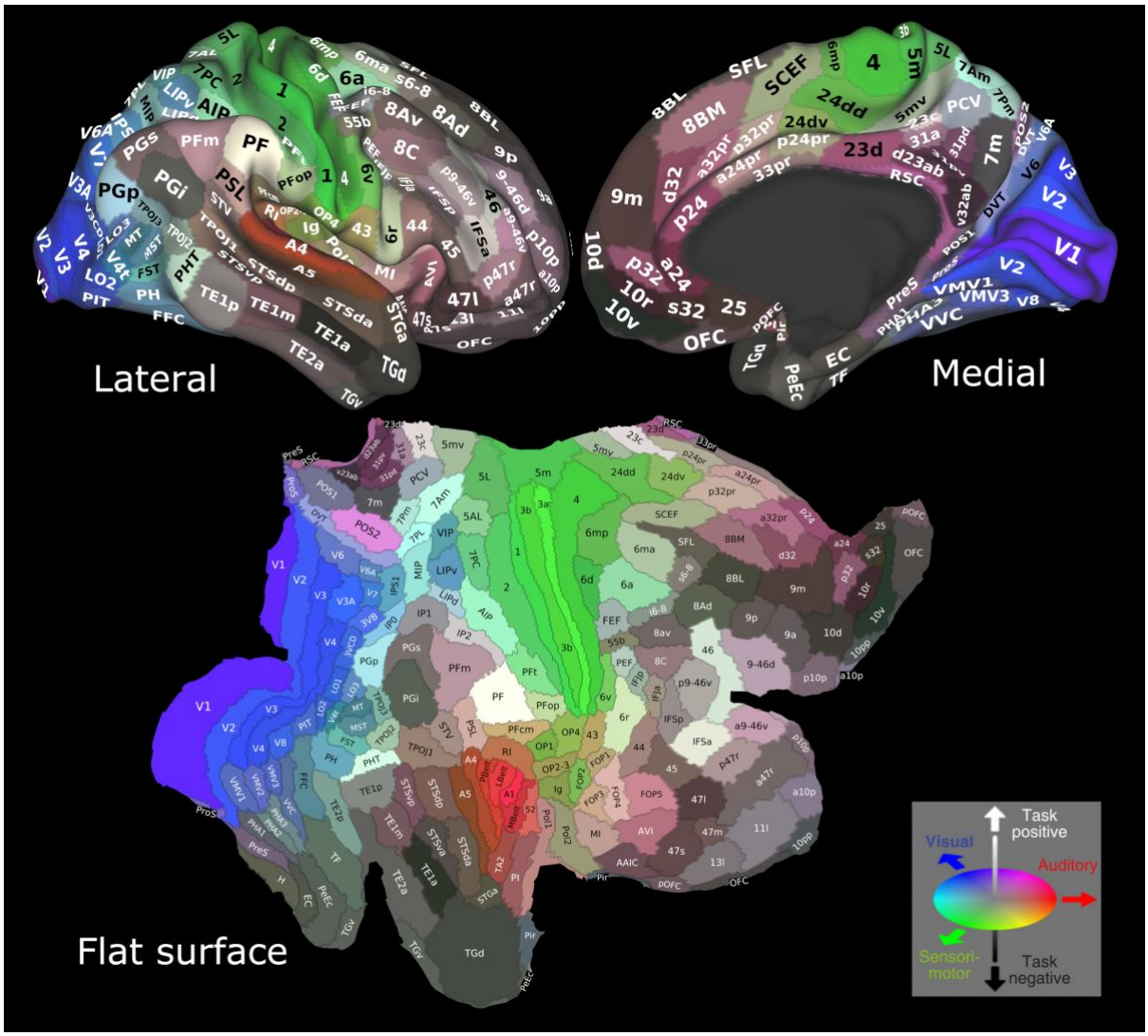

Figure 7. Parcellations of the right cerebral hemisphere. Parcellation of 180 anatomical brain areas by Glasser and collaborators (2016) mapped to partially inflated (midthickness, lateral and medial views) and flat brain surfaces for the right hemisphere. The diagram at the right bottom corner of the figure indicates the meaning of the underlying region/area color codes – modality in the horizontal plane and task-dependence in vertical direction. The complete list and the origin of abbreviations of brain areas are available in the 3rd supplementary file to Glasser et al., 2016 (*Supplementary neuroanatomical results*, Table 1).

Chapter 3. Results

This chapter is divided into two separate sections. In the first section the results from the main experiment are described, including the outcomes for particular stages of interactions with bimanual tools as compared to unimanual tools. The second part concerns the results of an additional experiment – the one in which participants had to adjust grasps prior to using bimanual or unimanual tools.

3.1 The results of the main project (Experiment 1)

3.1.1 Whole-brain analyses

3.1.1.1 Planning, grasping and using of bimanual and unimanual tools versus non-tools

Interaction with tools elicited activity within the fronto-parieto-temporal cortices in all three phases of the action: planning, grasping and using tools (see Figure 8). The results for each phase will be described in detail below, with two region (area) naming conventions: traditional names of particular sites across the brain (e.g.: premotor cortex, supramarginal gyrus), and with a multi-modal brain parcellation (as defined by Glasser et al., 2016; e.g.: 6r, 6v, or PFt).

As depicted in Figure 8 panel A and Figure 9, planning functional grasps of tools (both bimanual and unimanual) at the hand-independent level involved neural processing within the temporo-parieto-frontal set of brain regions. For this contrast, signal increases were observed mostly in the left hemisphere: in the postero-ventral temporal and lateral occipital areas (in the multi-modal parcellation notation, MMP, from TE1p to PHA3, but also encompassing V3B and V4), an extended activity along IPS (in MMP jargon: IP0 to AIP), a large portion of SPL (from DVT to 7PC) and merely an anterior part of IPL – aSMG (PFt and superior PF), in premotor cortices – PMv and PMd (6r, 6v, PEF, 6a, and 6ma), a PMv-adjacent cluster in IFG (IFJp and IFJa), extending through the inferior frontal sulcus – IFS (IFSp) to MFG (p9-46v and 46), as well as a cluster in medial-frontal areas – supplementary motor area – SMA (a32p, p32pr, 8BM, and SCEF). Nevertheless, there were also some contributions from the right hemisphere: ventral lateral occipital complex (LOC)/posterior inferior temporal gyrus – ITG (PH3 to V4 and V3CD, although less extended than in the left hemisphere), dorsal IPS, and in SPL (IPS1 to 7Am), and AIP along the medial wall of the intraparietal sulcus (AIP and LIPd). For a more detailed depiction, including MMP borders see also Figure 9.

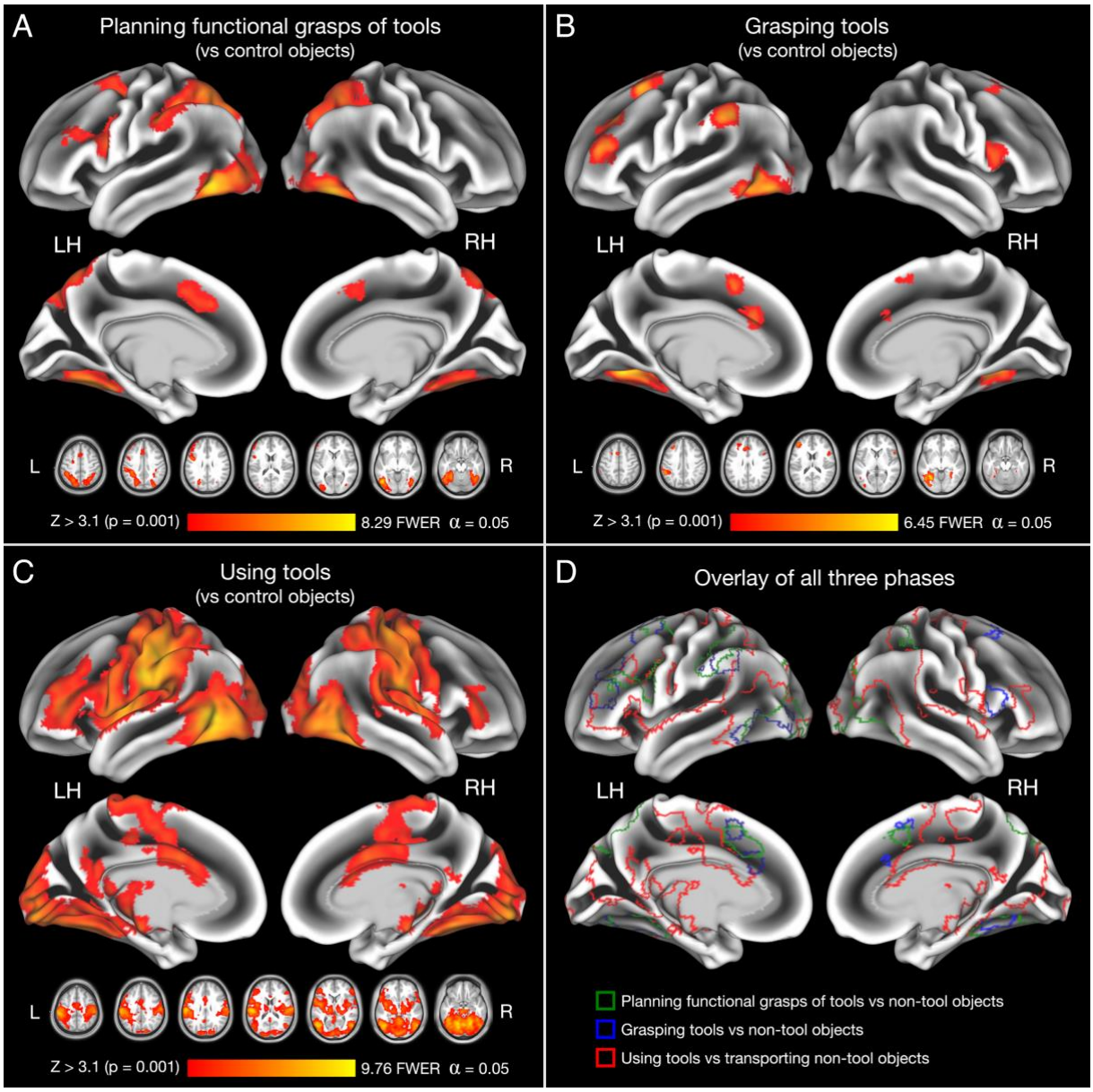

Figure 8. Hand-independent main effect of object type (tools vs. non-tools) from a 2×2×2 rmANOVA. There are three phases of action presented: (**A**) planning functional grasps; (**B**) grasping the tool; and (**C**) using the grasped tool. Overlays of the results for all stages of the action are presented in panel **D** as outlines: green for planning, blue for grasping, and red for using tools vs. non-tools. The statistical parametric maps presented in this figure come from a 2×2×2 whole-brain rmANOVA with the following factors: hand (left, right), manuality (unimanual, bimanual), and functionality (tool, non-tool). The results are mapped to partially inflated (midthickness, lateral and medial views) brain surfaces, as well as to 7 volumetric brain slices across the axial plane. Color maps and bars represent standardized (*Z*-scored) *t* statistics from the follow up (post-hoc) direct comparisons between the tool and non-tool conditions, thresholded above the 3.1 *Z* value. FWER stands for the family-wise error rate at a given alpha (α) level (0.05), i.e., a correction for the number of clusters.

As depicted in Figure 8 panel B and Figure 10, when participants proceeded to the execution of the preprogrammed grip in the *grasping* phase, signal increases were generally observed more ventrally than during planning. The significant clusters for grasping were located within the premotor and temporo-occipital areas (see Figure 8B and Figure 10). The overlay of planning and grasping phases is presented in Figure 8D and in Figure 11. More specifically, performing functional grasps of tools elicited neural activity within the left hemisphere parietal cortex restricted to more posterior subdivisions of SMG, and extending to IPS (MMP notation: PFt, PF, PFm, to IP2, and AIP). Within the frontal lobe, the clusters observed during grasping were smaller than when participants were planning the action (9-46d, 46, IFSa, p9-46v, and 8Ad). The activity within the left hemisphere was also observed in the dorsal premotor to medial-frontal areas (6a, 6ma, s6-8, SFL, SCEF, 8BM, a32pr, p32pr, and a32pr). Finally, for grasping there were also signal changes in the ventral postero-temporal and occipital cortices (VMV1 through activity peaks in VMV3 and PH to TE1p temporally, and LO1 and V4 occipitally), although these clusters were smaller than during grasp planning, especially in the occipital lobe. As for the effects observed in the right hemisphere during the grasping phase, there were four clusters of significant activity. The first was located in the ventral premotor cortex and inferior frontal gyrus (6r and 44). Then, there were three small clusters in the medial frontal regions (along: 6a, s6-8, SFL, SCEF, 8BM, and one cluster in a32pr). The strongest effect was observed in the ventral occipital areas (VMV2, VMV3, VVC, PH1, PH2, and PH3). As before, the results for the grasping phase presented in Figure 8B (partially inflated surfaces and volumetric slices) are followed by a more detailed depiction in Figure 10 (flattened brain surface with MMP borders).

The intersections of clusters of significant effect for the first two phases of the interaction – planning and grasping – were observed across the following left-hemispheric brain lobes: frontal (IFS: IFSa and 46; dorsal ventral to medial frontal areas: 6a to a32pr), parietal (SMG: PF to AIP), temporal and occipital (ventral PHA3 to V4 and LO1). The overlay of both: planning and grasping phases is shown in Figure 11. There were also analogous intersections within the right hemisphere, but the effects barely reached the significance level, and the cluster sizes were much smaller than in the left hemisphere (tens as compared to hundreds and thousands of voxels). Additionally, it was the left hemisphere that I was primarily interested in; hence, given the obtained results, the overlay in the right hemisphere is not visualized. Yet, the reader can inspect Figure 8, panel D, for the overview of the intersections of planning and grasping in the right hemisphere.

As depicted in Figure 8C, during the execution phase (the actual tool use), there were massive effects across both the left and right hemisphere. The effects observed during execution were more extended and stronger than during both planning and grasping. As the main scope of this thesis are functional grasp-preparatory processes, not the tool-use *per se*, the results for tool-use execution are not reported here in detail; they are only visualized in Figure 8C. Additionally, as mentioned before, the overlay of all three phases, including tool-use, is presented in Figure 8D.

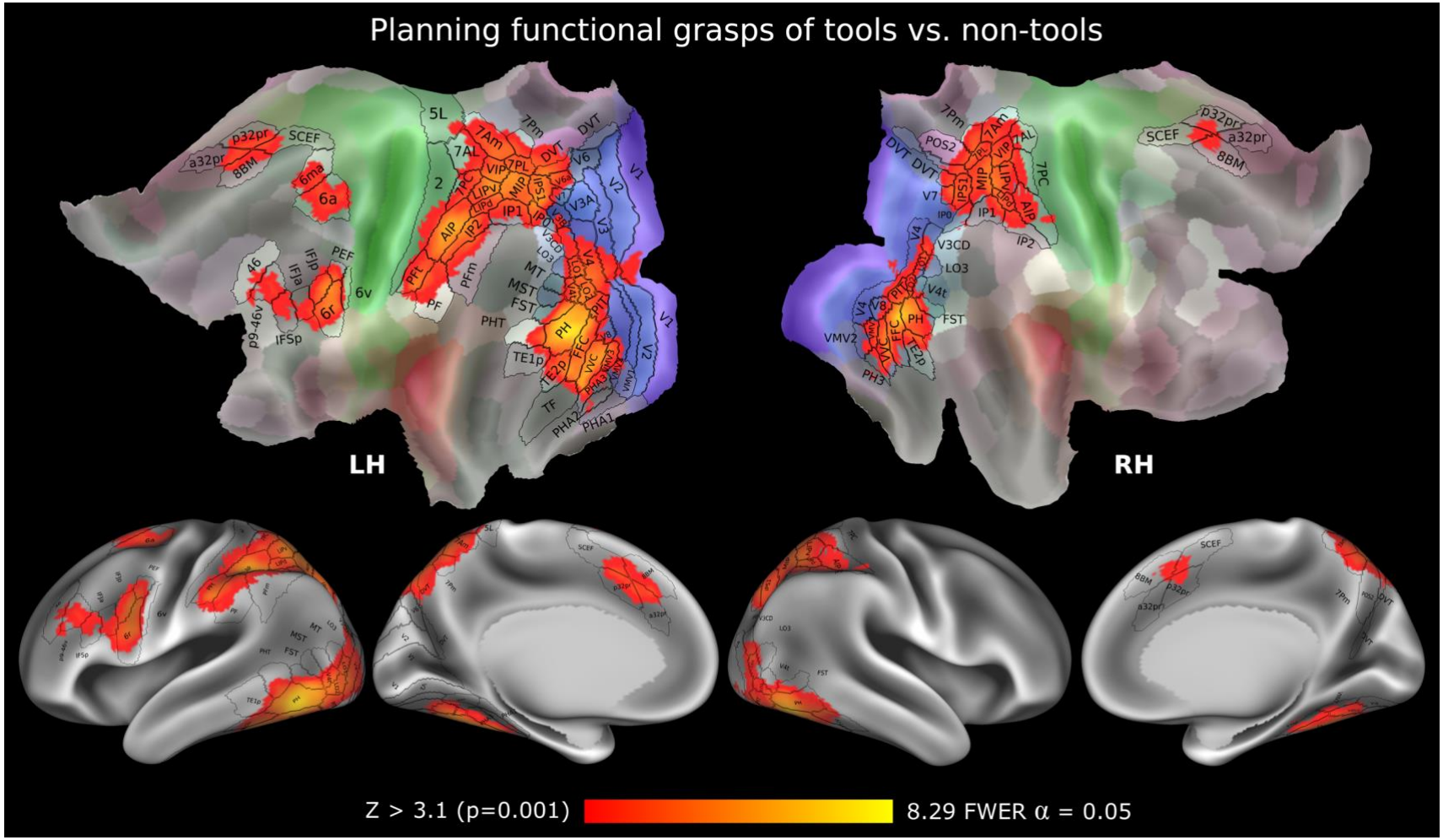

Figure 9. Hand-independent main effect of object type (tools vs. non-tools) for the planning phase from a 2×2×2 rmANOVA. The statistical parametric maps involve the following rmANOVA factors: hand (left, right), manuality (unimanual, bimanual), and functionality (tool, non-tool). In the upper row there are flattened brain surfaces with the color coded, transparent underlay of multi-modal parcellation for the 180 brain regions (Glasser et al., 2016). In the bottom row the results are mapped to partially inflated (inflated midthickness, lateral and medial views) brain surfaces. The left hemisphere is visualized on the left, and the right hemisphere on the right. Color maps and bars represent standardized (Z-scored) *t* statistics from the follow up (post-hoc) direct comparisons between the tool and non-tool conditions, thresholded above the 3.1 Z value. FWER stands for the family-wise error rate at a given alpha (α) level (0.05), i.e., a correction for the number of clusters.

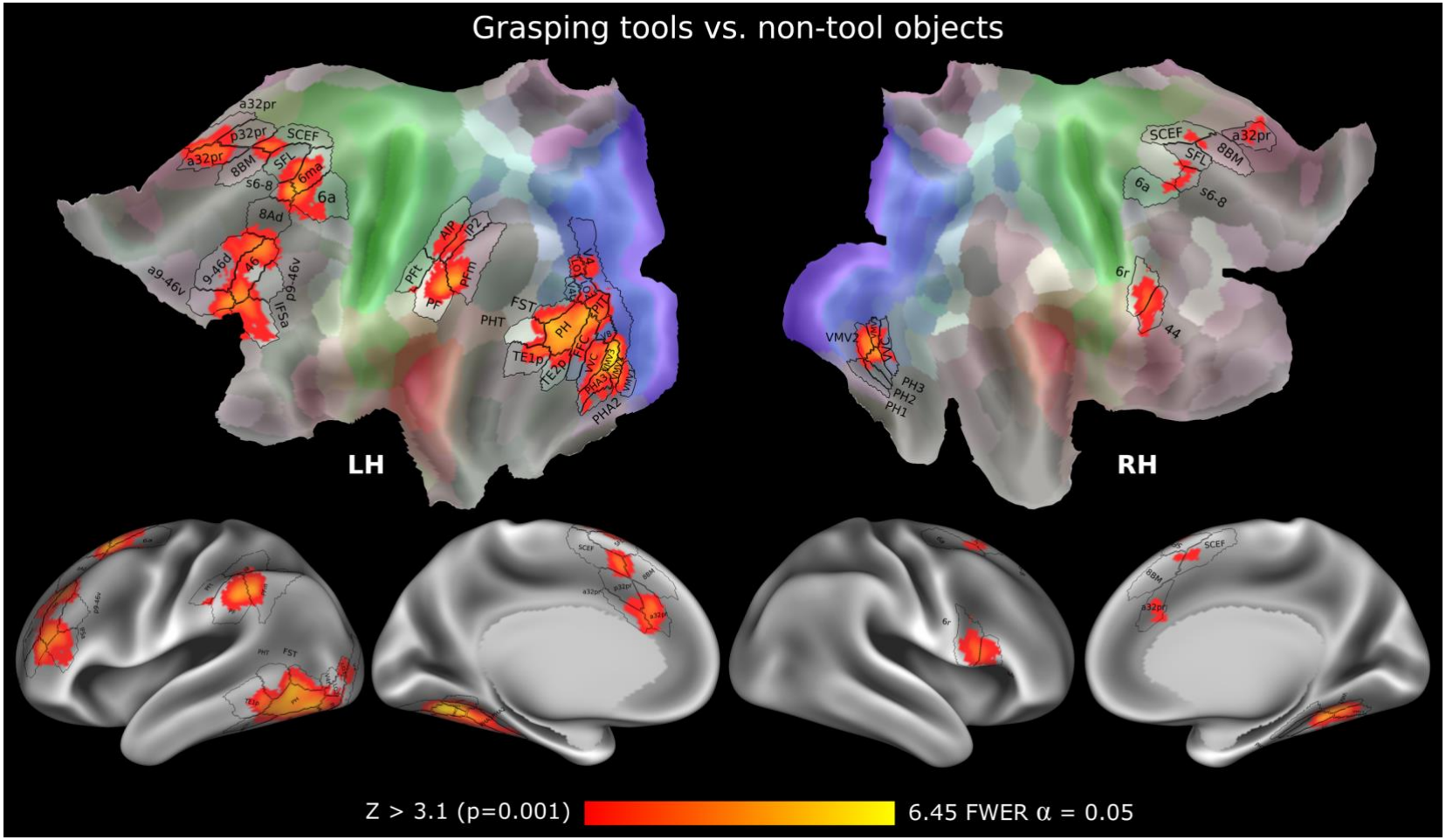

Figure 10. Hand-independent main effect of object type (tools vs. non-tools) for the grasping phase from a 2×2×2 rmANOVA. The statistical parametric maps involve the following rmANOVA factors: hand (left, right), manuality (unimanual, bimanual), and functionality (tool, non-tool). In the upper row there are flattened brain surfaces with the color coded, transparent underlay of multi-modal parcellation for the 180 brain regions (Glasser et al., 2016). In the bottom row the results are mapped to partially inflated (inflated midthickness, lateral and medial views) brain surfaces. The left hemisphere is visualized on the left, and the right hemisphere on the right. Color maps and bars represent standardized (Z-scored) *t* statistics from the follow up (post-hoc) direct comparisons between the tool and non-tool conditions, thresholded above the 3.1 Z value. FWER stands for the family-wise error rate at a given alpha (α) level (0.05), i.e., a correction for the number of clusters.

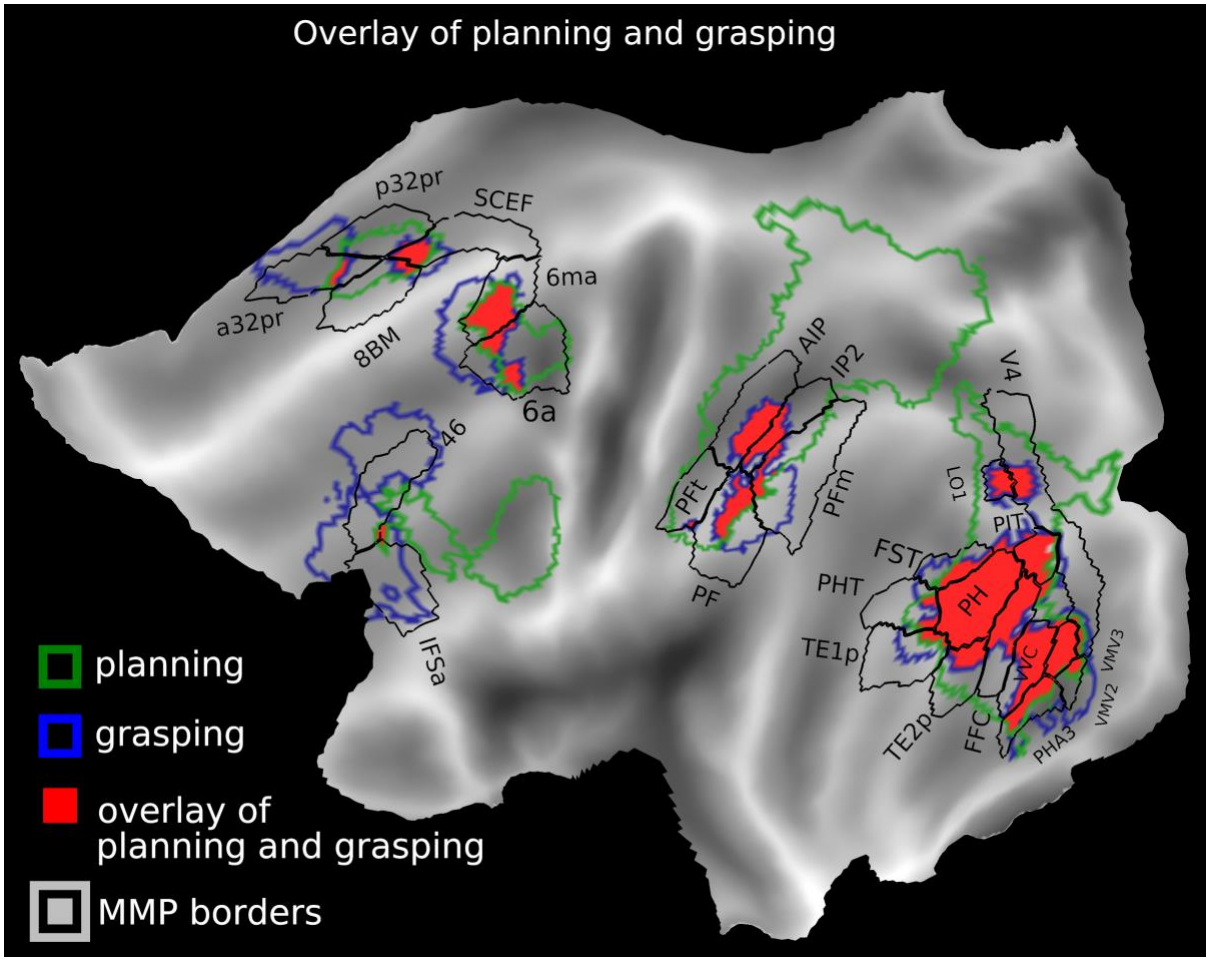

Figure 11. An overlay for a hand-independent main effect of object type (tools vs. non-tools) for planning and grasping phases from a 2×2×2 rmANOVA involving hand (left, right), manuality (unimanual, bimanual), and functionality (tool, non-tool). The outlines represent statistical parametric maps shown on the flattened brain surface of the left hemisphere. Green outlines represent a border for a statistically significant effect for the planning phase, blue overlay stands for grasping. Red-filled areas represent places where the two effects intersect, while black borders and accompanying labels represent brain areas as defined by multi-modal parcellations (Glasser et al., 2016).

3.1.1.2 Planning, grasping and using of bimanual versus unimanual tools with rest as reference

In this section a direct comparison between bimanual and unimanual tools will be presented. Noteworthily, the results presented here come from comparisons with rest intervals, i.e., the signals related to control objects were not subtracted in this rmANOVA, and these objects were not included, either. (For the results where contrasts with control objects were utilized, see the next section.)

The main thesis posed in this dissertation is that the neural underpinnings of planning interactions with bimanual tools differ from the representations of planning actions with unimanual tools, as observed in the fMRI. In order to address this research question, the two first phases distinguished in my experimental paradigm are essential: grasp planning and grasp execution. Because I was primarily interested in tools, the results presented here will be restricted to tool-related effects.

As shown in Figure 12 panel A and Figure 13 panel A, during the planning phase, a statistically significant main effect of tool type (bi- vs. unimanual) was revealed exclusively in the right hemisphere. The effect was observed in SPL, postcentral sulcus, and to the lesser extent in the central sulcus (see Figure 12A; from area 4 as delineated in MMP – anteriorly, to VIP and LIPv – posteriorly, see also Figure 13A).

Grasping, on the other hand, engaged bilateral motor and somatosensory areas (6d to 7PC), some bilateral inputs from the visual cortex (V1 and V3A dorsally; and V1, V2, and V3 ventrally), and, restricted to the right hemisphere – parietal sites: SPL and dorsal IPS (POS2, through AIP to 7PC). Moreover, the MT/MST complex also contributed to the observed effect, but only in the right hemisphere (see Figure 12B and Figure 13B).

Finally, functional tool use invoked neural processing bilaterally, again within the somatosensory areas, as well as in visual, and prefrontal cortices (with the more pronounced activity within the left hemisphere; see Figure 12C, MMP borders are not presented here). The overlay of the activity outlines from all three phases of the studied interaction with tools (bimanual, unimanual) is presented on the midthickness brain surface in Figure 12D, and the intersection of grasp-related phases (planning and grasping) is presented on the flattened brain surface in Figure 14.

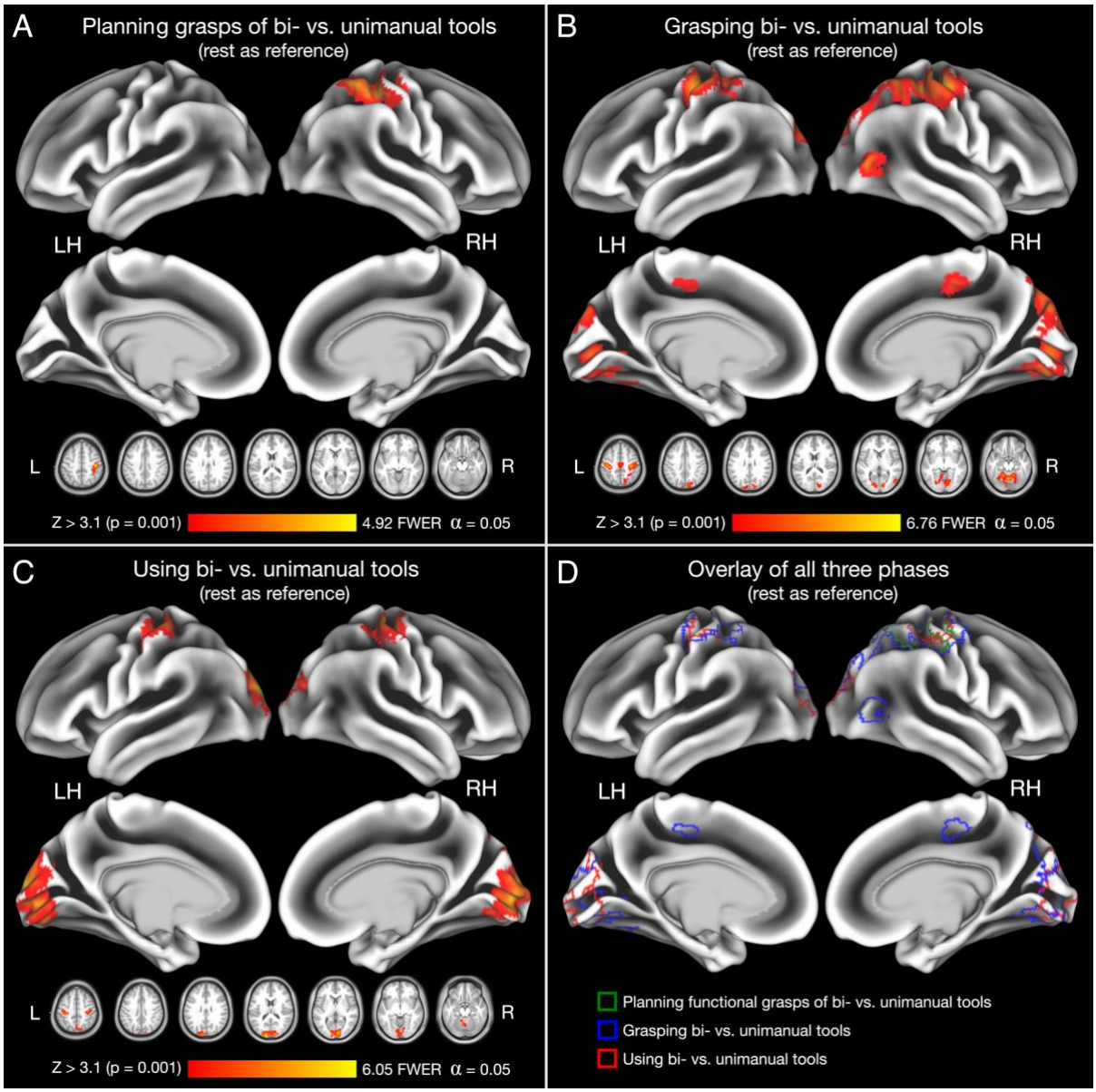

Figure 12. A main effect of tool type (bi- vs. unimanual) from an rmANOVA with rest as reference. The results presented here are statistically significant clusters (based on parametric maps) from *t*-tests, performed following a 2×2 rmANOVA with the following factors: manuality (unimanual, bimanual), and hand (left, right). This analysis was restricted to tools only and the inputs to the analysis were contrasts of tool-related conditions with rest periods. Only hand-independent results are presented, i.e., the results are collapsed across the hand factor. There are three phases of action presented here: planning functional grasps (**A**), grasping tools (**B**), and using the grasped tools (**C**). The overlay of the results for all stages of the action is presented on the midthickness surface in panel **D**. The results are mapped onto partially inflated (lateral and medial views) brain surfaces, as well as 7 brain slices across the axial plane. Color maps and bars represent standardized (Z-scored) *t* statistics from the follow up (post-hoc) direct comparisons between the bimanual and unimanual tool conditions, thresholded above the 3.1 Z value. FWER stands for the family-wise error rate at a given alpha (α) level (0.05), i.e., a correction for the number of clusters.

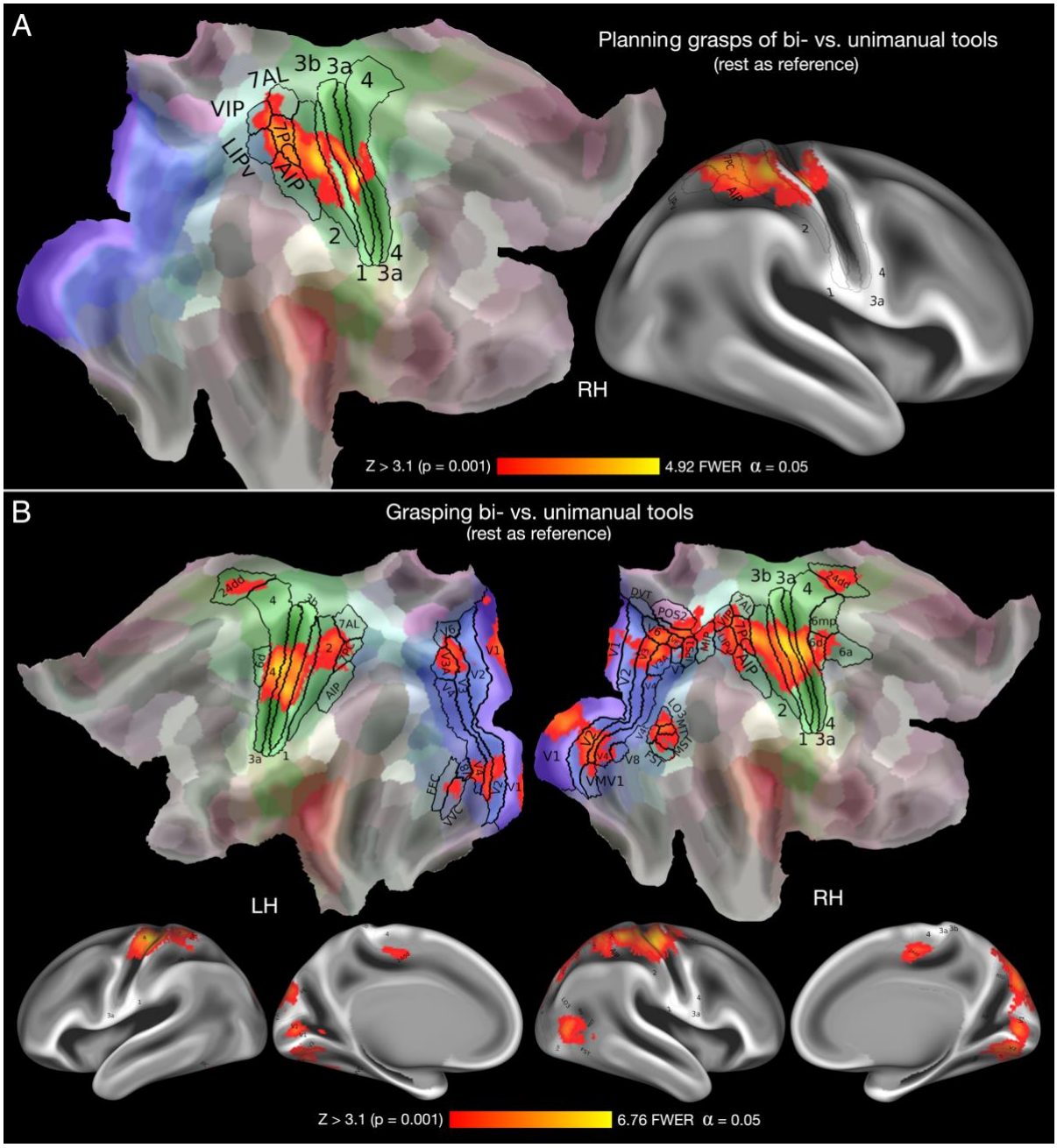

Figure 13. A main effect of tool type (bimanual vs. unimanual) from rmANOVA with rest as reference for the planning and grasping phases. In the upper panel (**A**) there are flattened (left side of the panel) and partially inflated surfaces presented, with a statistically significant main effect of tool type (bi- vs. unimanual). Only the right hemisphere is shown because there were no statistically significant voxels in the left hemisphere. Grasping the object (**B**) is also presented on two surfaces, flattened (upper row of the panel), and partially inflated (bottom row). Black borders represent a multi-modal parcellation (MMP, see Glasser et al., 2016). Color maps and bars represent standardized (Z-scored) *t* statistics from the follow up (post-hoc) direct comparisons between the bimanual and unimanual tool conditions, thresholded above the 3.1 Z value. FWER stands for the family-wise error rate at a given alpha (α) level (0.05), i.e., a correction for the number of clusters.

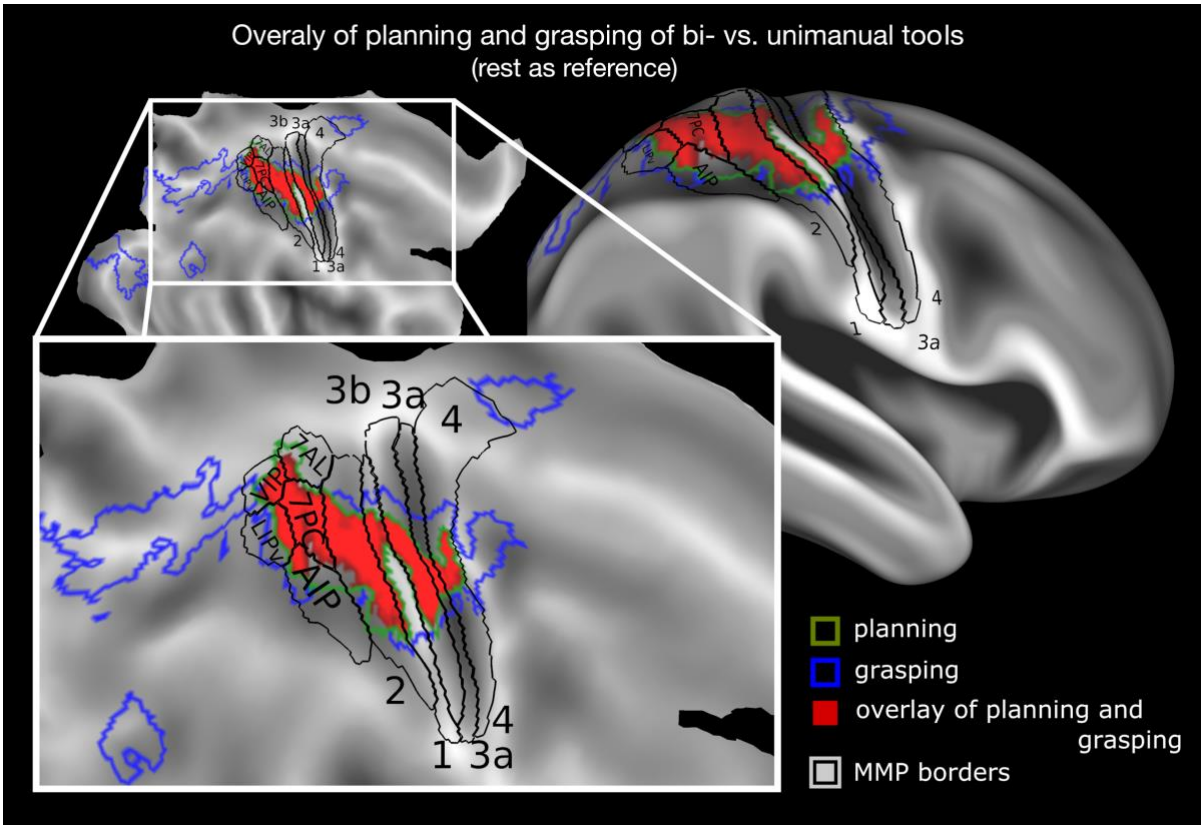

Figure 14. A main effect of tool type (bimanual vs. unimanual) from an rmANOVA with rest as reference: an overlay for the planning and grasping phases. The intersection of planning and grasping-related activity is presented here. Only the right hemisphere is shown because the planning-related effect was revealed only in the right hemisphere. Green outlines represent the planning phase, blue outlines the grasping phase, and the intersection is marked in red. Black labelled outlines represent a multi-modal parcellation (MMP, see Glasser et al., 2016).

3.1.1.3 Planning, grasping and using bimanual versus unimanual tools with control objects as reference

When the inputs for the ANOVA were contrasts of tools vs. non-tools, three significant clusters were revealed in a main effect of tool type (bimanual vs. unimanual). For planning functional grasps, these clusters were located exclusively in the right hemisphere, more specifically: in the superior parietal lobule (MMP: 7PC, and in its immediate vicinity: AIP, LIPv, VIP, and 7AL), in somatosensory (2, 1, 3a, 3b) and in motor cortices (area 4). These results are presented in Figure 15A (on midthickness – partly inflated – surfaces), and in Figure 16A (flattened, and more inflated surfaces, with additional parcellation borders also mapped).

Grasping tools engaged more extensive clusters than planning, additionally involving the left hemisphere. The statistically significant effects for grasping extended from the sensorimotor cortices, through SPL, to dorsal IPS (MMP: 6d to 7PC; with greater involvement of the right hemisphere). There were also smaller clusters in the medial motor cortex bilaterally (in 24dd), as well as some foci of activity within the visual cortex, restricted almost exclusively to the right hemisphere (V1, V2/V3, and a cluster in the V3A/V6 vicinity; whereas in the left hemisphere there was only a small cluster within the V3). For the visualization of these outcomes see Figure 15B (midthickness inflated surfaces) and Figure 16B (flattened, and more inflated surfaces with MMP borders also indicated). The overlay of both planning and grasping phases is presented in Figure 17, with MMP borders mapped onto the delineated effects.

During bimanual tool use only the left hemisphere was engaged, with activity focused in somatosensory and early dorsal visual cortices (as shown in Figure 15C; no flattened maps for this phase). All three stages of the interaction with tools are presented altogether in Figure 15D.

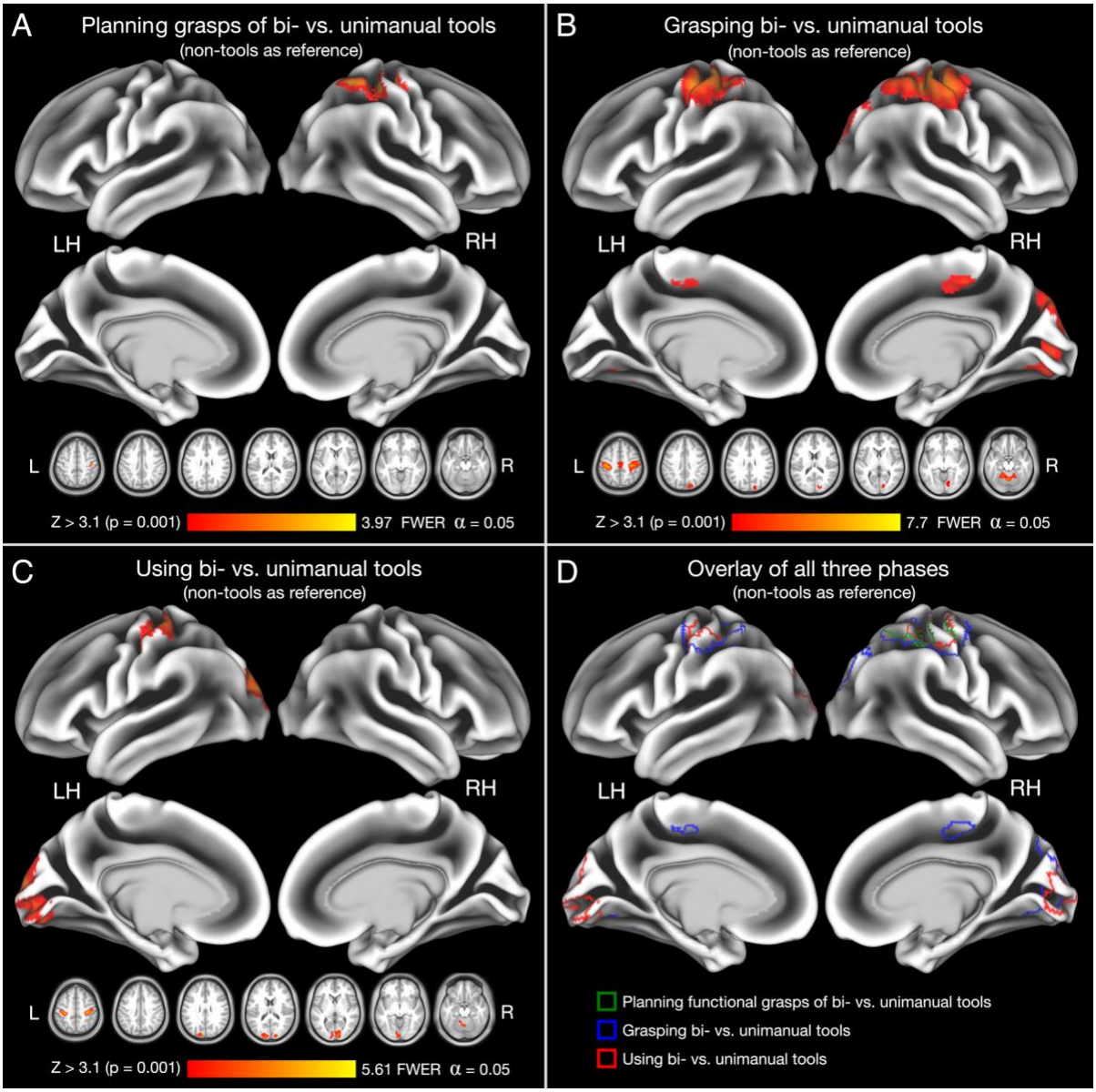

Figure 15. A main effect of tool type (bimanual vs. unimanual) from an rmANOVA, with control objects (non-tools) as reference. The three phases of action are presented here: planning functional grasps (**A**), grasping the object (**B**), and using the grasped object (**C**). Overlay of the results for all stages of the action is presented on surfaces in panel **D**. The results are mapped to partially inflated (midthickness, lateral and medial views) brain surfaces, as well as 7 brain slices across the axial plane. Color maps and bars represent standardized (Z-scored) *t* statistics from the follow up (post-hoc) direct comparisons between the bimanual and unimanual tool conditions, thresholded above the 3.1 Z value. FWER stands for the family-wise error rate at a given alpha (α) level (0.05), i.e., a correction for the number of clusters.

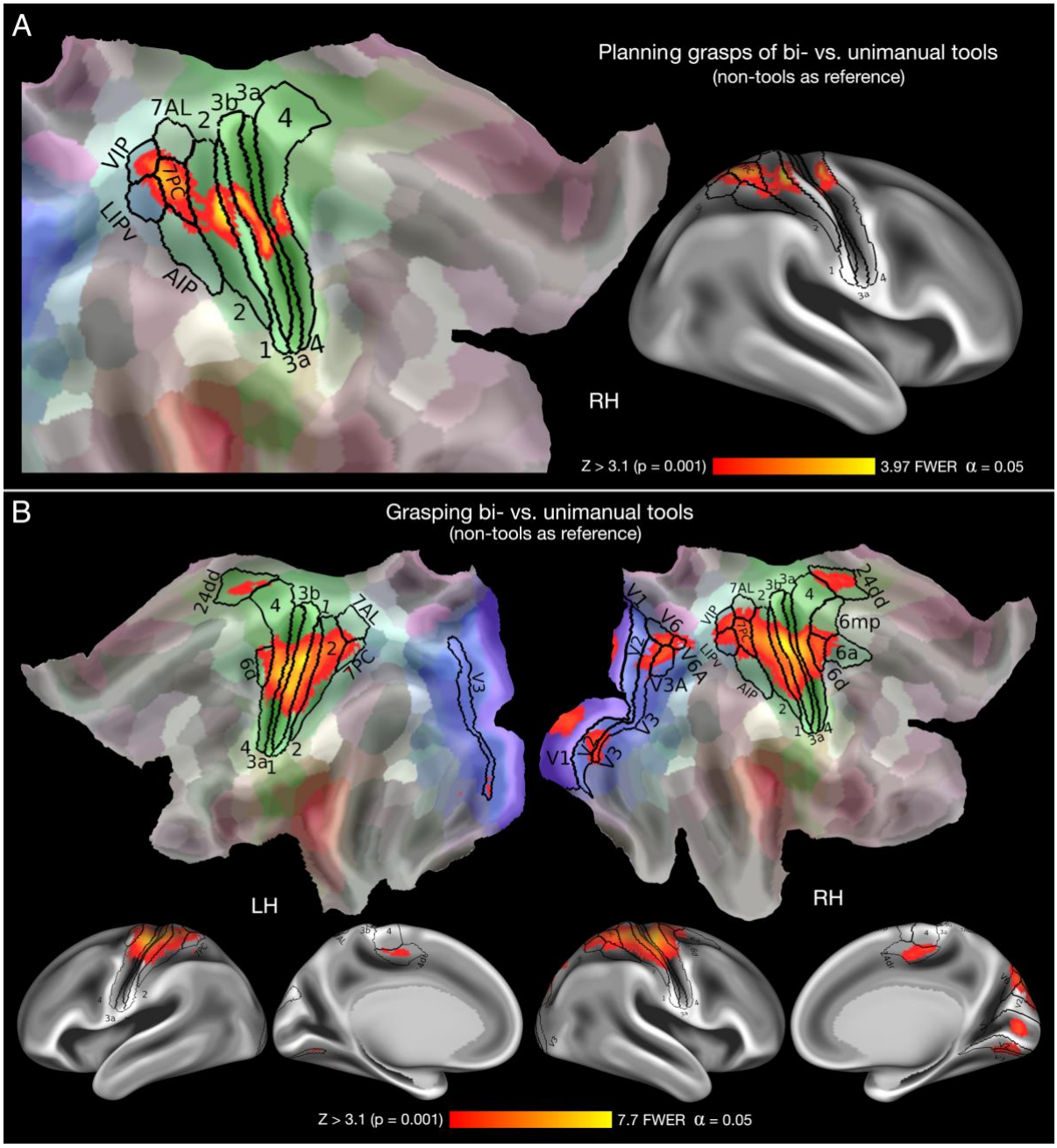

Figure 16. A main effect of tool type (bimanual vs. unimanual) from an rmANOVA with non-tools (control objects) as reference for the planning and grasping phases. In the upper panel (**A**) there are flattened (left side of the panel) and partially inflated surfaces presented with statistically significant effects for tool type (bi- vs. unimanual). Only the right hemisphere is shown here because there were no statistically significant clusters in the left hemisphere. Grasping the object (**B**) is also presented on both flattened (upper row in the panel) and partially inflated surfaces (bottom row). Black borders represent a multi-modal parcellation (MMP, see Glasser et al., 2016). Color maps and bars represent standardized (Z-scored) *t* statistics from the follow up (post-hoc) direct comparisons between the bimanual and unimanual tool conditions, thresholded above the 3.1 Z value. FWER stands for the family-wise error rate at a given alpha (α) level (0.05), i.e., a correction for the number of clusters.

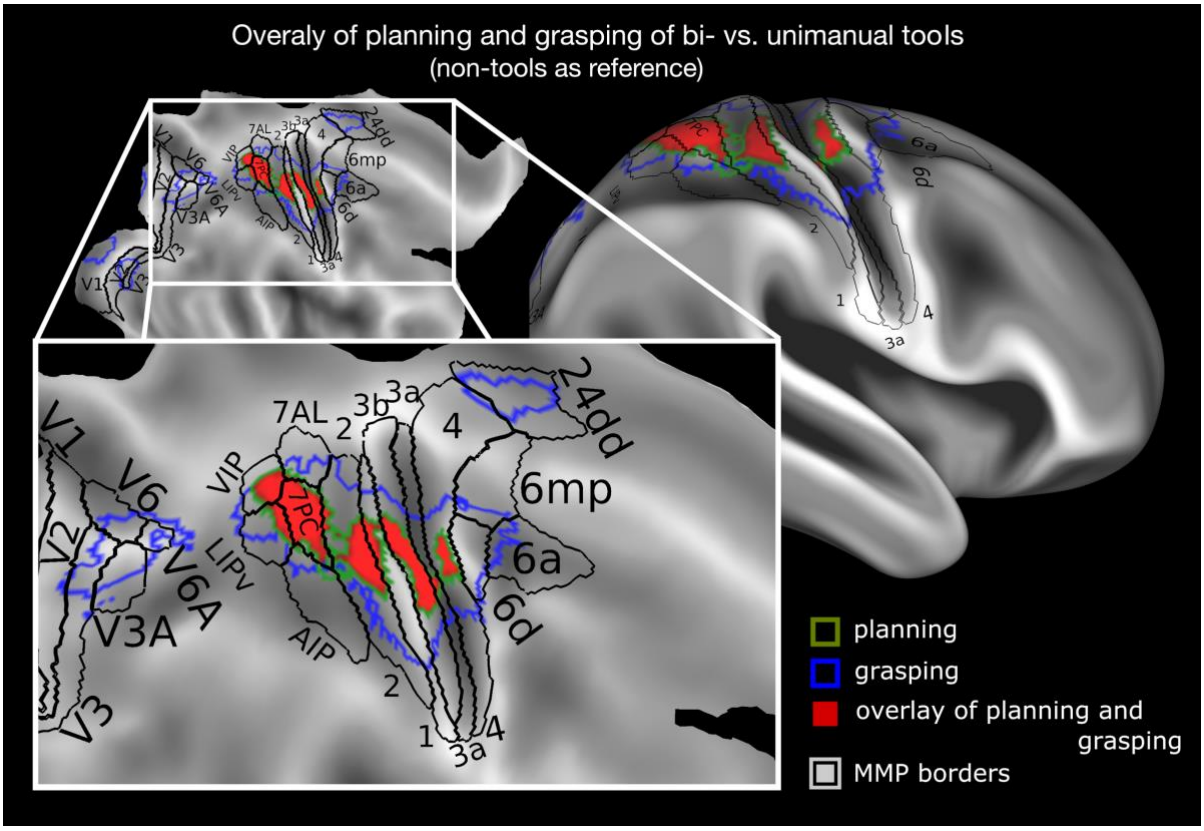

Figure 17. A main effect of tool type (bimanual vs. unimanual) from an rmANOVA with non-tool objects as reference: an overlay of the planning and grasping phases. The intersection of planning and grasping-related activity is presented in this figure. Only the right hemisphere is shown because planning-related effects were revealed only in the right hemisphere. Green outlines represent the planning phase, blue outlines the grasping phase, and the intersection is marked in red. Black labelled outlines represent a multi-modal parcellation (MMP, see Glasser et al., 2016).

3.1.2 Conjunction analyses

The more general conjunction test – (BiToolRight > UniToolRight) ∩ (BiToolRight > BiControlRight) ∩ (UniToolRight > UniControlRight) – did not reveal any statistically significant activity. Interestingly, the more specific, bimanual effect was observed in the second conjunction that was performed, i.e., (BiToolRight > UniToolRight) ∩ (BiToolRight > BiControlRight). Nevertheless, the observed outcome was statistically significant just above the 3.1 *Z* threshold (*Z* max at 3.54). Therefore, to provide a more general overview of this effect, the *Z* threshold was lowered to a more liberal, 2.3 value. As presented in Figure 18, the bimanual tool-specific effect was revealed as a single large cluster, located mainly in the right superior parietal lobule (MMP: spanning from V7 and V6A, through DVT, POS2, 7PL, 7Pm and 7Am, to 7AL and 5L), and in the medial wall of the intraparietal sulcus (MIP, VIP, LIPv, LIPd, AIP, and IPS2).

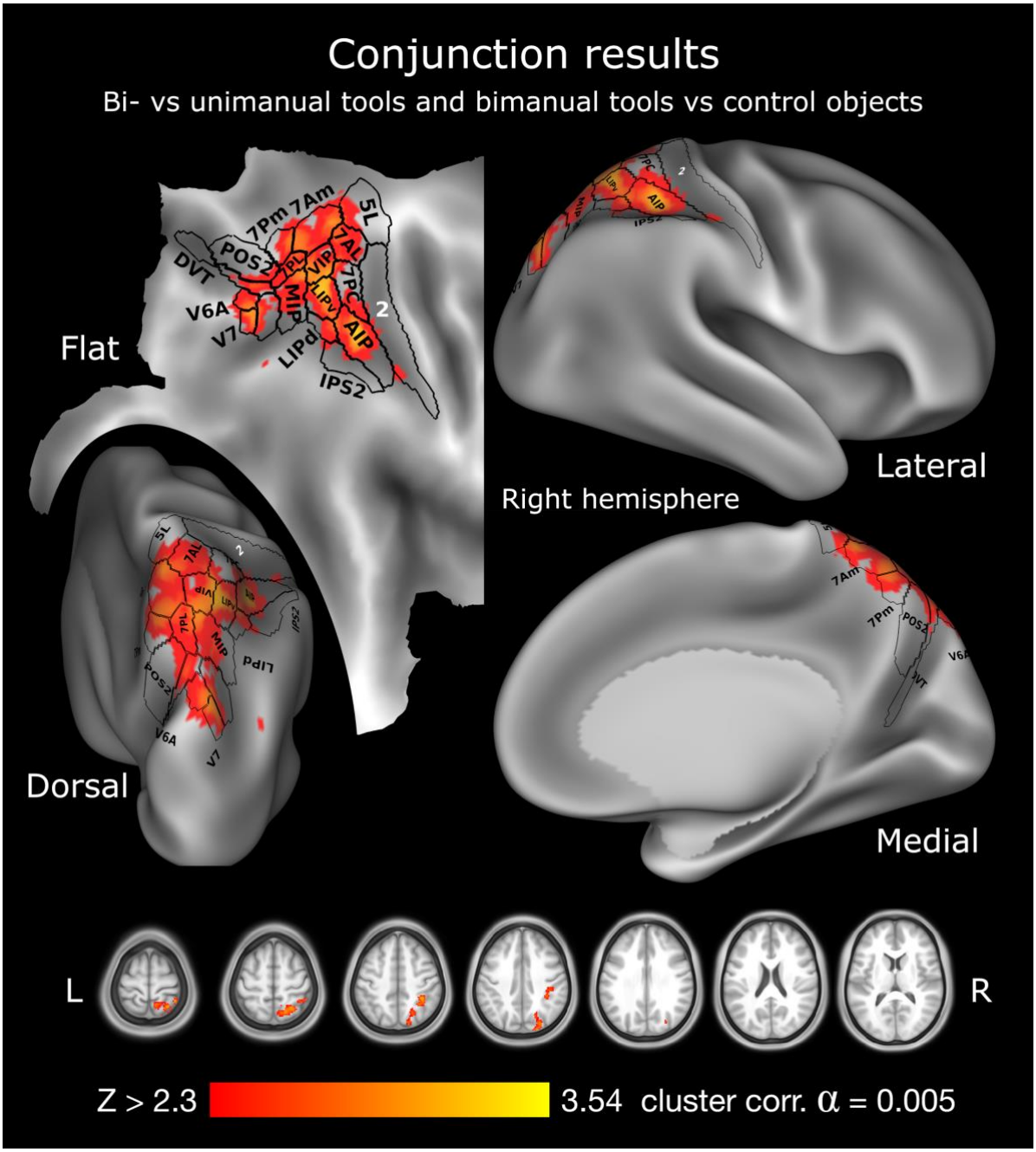

Figure 18. A conjunction analysis result – an effect specific to bimanual tools. Results of the (BiToolRight > UniToolRight) ∩ (BiToolRight > BiControlRight) conjunction analysis are shown. The threshold for the presentation of the result was lowered to Z > 2.3.

3.1.3 ROI analyses

The main purpose of utilizing the ROI approach was to account for the signal variability in critical PRN nodes. There should be signal fluctuations, as the interaction with the tools progressed, from planning, through grasping, to finally using tools. The results of the ROI analyses revealing this transition are presented in Table 2 and Table 3.

Consistently with a general intuition on the activity within PRN (based on the whole-brain contrasts presented above), the *leading* hand did not contribute significantly to signal variability. Namely, only PMd (in both analyses) and cSPL (when referenced to control objects) seemed to be sensitive to hand dominance effect. In other words, there was relatively little difference whether participants performed the task with the right (dominant) hand or with the left (non-dominant) hand. In sharp contrast, signals from bimanual and unimanual tools were characterized by increased BOLD fluctuations in temporal, premotor, and frontal cortices. Surprisingly, no statistically significant differences between these conditions were observed in anterior intraparietal areas. All the selected regions showed high sensitivity to a general category of tool type (tools vs. non-tools), when this condition was considered (relative to resting activity, see Table 2), as all of these ROIs are parts of PRN which represents, among other aspects of tool use, object functionality. Finally, when the three phases of the task (*planning*, *grasping*, and *execution*) were considered, although the percent signal changes reached significance level in all analyzed ROIs for rest intervals as reference, and half of the regions for non-tools as reference, the brain region that was revealed as most active in both analyses is PMd (rest: $p<0.001$, PES = 0.63, OP = 1.0; control: $p<0.001$, PES = 0.48, OP = 0.92).

A similar trend can be observed for cMTG when the *manuality* factor (bimanual, unimanual), regardless of object type (tool, non-tool) is considered – no matter what reference is used. Indeed, signal fluctuations within this region have the greatest magnitude (rest: $p<0.01$, PES = 0.33, OP = 0.83; control: $p<0.001$, PES = 0.43, OP = 0.94). Interestingly, as far as the resting baseline activity is considered, cSPL was the region for which the highest number of interactions between factors was revealed. This shows that cSPL is involved in most refined signal processing, depending on the interplay of object function, kind and number of effectors, and stage/phase of the task. These interaction effects were non-existent when the neural activity from control tasks was accounted for. Nevertheless, for contrasts with control objects as reference, aSMG and cMTG showed the interactions of *hand* and *manuality* factors. This discrepancy indicates that tools alone invoke the ventro-dorsal and ventral stream of processing,

while the dorso-dorsal cSPL participates in differentiating between and processing of functional (*tools*) and non-functional (*control*) objects.

The results presented in Table 2 and Table 3 provide a comprehensive overview of the nature of the interaction with bimanual and unimanual tools, taking into account also the phase of the task, the *leading* hand, and information whether the action was performed with tools or non-tools. The more in-depth presentation of the ROI analysis results is available in Figure 19 and Figure 20, where the results were restricted to bimanual tools only, and were split into the right (dominant) and the left (non-dominant) hand.

For rest intervals as reference, in the case of both hands, comparisons between different stages of the task revealed differentiated signal percent changes along the dorso-dorsal stream of processing, namely in cSPL and PMd. As the action progressed from grasp planning, through grasping to functional tool use, percent signal changes decreased in cSPL. Meanwhile, in PMd the changes during the planning phase were evidently lower than during grasping and using a tool, i.e., percent signal changes increased as the action progressed (with the exception of tool use with the non-dominant hand; see Figure 19 for visualization). Moreover, for the non-dominant hand percent signal changes in rMFG were the highest during the grasping phase, as compared to grasp planning or tool use. Hence, the percent signal change patterns were similar for PMd and rMFG for the non-dominant (left) hand, which was not exactly the case for the dominant (right) hand.

When control objects were used as reference for signal change, only three ROIs showed significant differences between task phases for bimanual tools (as depicted in Figure 20). Percent signal changes within PMd were lower for grasping than during functional grasp planning, and even tool use, when the dominant (right) hand was considered (actually the signal was even lower than for control objects there – not presented here). For the non-dominant (left) hand two areas showed significant differences, namely, cMTG – signal changes during grasp planning were lower than during tool use, and cSPL – signal changes during grasp planning were higher than during performance of functional grasps of bimanual tools.

Broadly speaking, percent signal change was on average three times higher when rest was the reference (greater signal variability), as compared to the baseline comprising of control non-tool objects. It is not surprising, given the fact that interactions with control object closely resembled the situation when participants were planning grasps, then grasping, and finally using the bimanual tools. On the other hand, the advantage of using rest intervals as baseline was such that it seemed to bring forward more of an object-specific characteristics of brain activity (with the functional aspects the object being of secondary interest).

Table 2. Region of interest (ROI) analysis results with rest as a reference. Inputs for this analysis were parameter maps from the second level of the analysis (averaged for each participant), as referenced to resting periods (similarly to Figure 12), rather than control objects (for these results see Figure 15 and Table 3). Functional ROIs that were used to perform this analysis were obtained from the study by Przybylski and Kroliczak (2017). The regions were spherical masks of 5-mm radius, centered at peak voxels for the planning of functional grasps of tools contrasted with control objects. The table presents MNI coordinates of these voxels, their maximal *Z* values and results of the ROI analysis performed on the data from the current experiment (interactions with bimanual and unimanual objects). Here, as well as in the study by Przybylski and Kroliczak (2017) ROIs functionally defined for the right hand were used for extracting percent signal change for the right-hand condition in the current study (and *vice-versa* for the left hand). In other words, although locations of the two ROIs are provided in the table below, values that were subject to the ROI analysis were obtained separately for the right hand and left hand. Abbreviations of experimental conditions and statistical terms are described below the table.

		MNI coordinates								
Left hemisphere region	Hand	x	y	z	Peak Z value	Main effect of hand (right, left)	Main effect of manuality (uni-, bimanual)	Main effect of functionality (tool, control)	Main effect of task (plan, grasp, exec.)	Interactions
Caudal middle temporal gyrus (cMTG) lateral occipital (LO) cortex	Right Left	– 48 – 42	– 66 – 72	– 2 – 4	4.2 4.37	0.37	** PES = 0.33, OP = 0.83	*** PES = 0.87, OP = 1.0	* PES = 0.21, OP = 0.71	(H × M)*** PES = 0.57, OP = 0.99 (T × F)* PES = 0.33, OP = 0.95 (M × F)*** PES = 0.85, OP = 1.0 (H × M × F)$^{p<0.068}$ PES = 0.17, OP = 0.45
Anterior supramarginal gyrus (aSMG)	Right Left	– 54 – 52	– 34 – 34	38 36	5.42 5.15	0.16	0.33	*** PES = 0.81, OP = 1.0	*** PES = 0.33, OP = 0.97	(T × F)* PES = 0.17, OP = 0.58 (M × F)*** PES = 0.76, OP = 1.0 (H × M × F)* PES = 0.25, OP = 0.67 (H × M)$^{p<0.058}$ PES = 0.18, OP = 0.48
Caudal superior parietal lobule (cSPL)	Right Left	– 12 – 18	– 74 – 74	48 50	4.23 4.3	0.47	0.16	*** PES = 0.65, OP = 1.0	** PES = 0.29, OP = 0.84	(H × M)** PES = 0.42, OP = 0.94 (H × F)* PES = 0.27, OP = 0.71 (T × F)** PES = 0.19, OP = 0.64 (M × F)*** PES = 0.76, OP = 1.0 (T × M × F)* PES = 0.16, OP = 0.64
Ventral premotor cortex (PMv)	Right Left	– 58 – 54	2 2	38 32	4.46 4.91	0.1	* PES = 0.29, OP = 0.75	*** PES = 0.53, OP = 0.99	*** PES = 0.31, OP = 0.95	(M × F)** PES = 0.38, OP = 0.85 (H × M)$^{p<0.099}$ PES = 0.14, OP = 0.38 (T × F)$^{p<0.092}$ PES = 0.13, OP = 0.45
Dorsal premotor cortex (PMd)	Right Left	– 22 – 26	–14 – 14	64 56	5.26 4.67	** PES = 0.42, OP = 0.94	** PES = 0.35, OP = 0.85	*** PES = 0.76, OP = 1.0	*** PES = 0.63, OP = 1.0	(H × T)* PES = 0.18, OP = 0.62 (H × M)*** PES = 0.69, OP = 1.0 (M × F)*** PES = 0.83, OP = 1.0 (T × F) $^{p<0.076}$ PES = 0.15, OP = 0.45
Rostral middle frontal gyrus (rMFG) (right hand from inclusive contrast)	Right Left	– 36 – 36	36 36	30 30	2.75 4.07	0.36	* PES = 0.22, OP = 0.6	*** PES = 0.64, OP = 1.0	*** PES = 0.38, OP = 0.98	(H × T × F)* PES = 0.16, OP = 0.62 (M × F)** PES = 0.42, OP = 0.94

Note. The goal of the ROI analysis performed here (after Kroliczak & Frey, 2009, and Przybylski & Kroliczak, 2017) was to test for differences and direction of amplitude (%) signal changes in conditions relative to the baseline brain state during resting. Variance of the signal within each ROI was explained by either the main effect of the factors, or interactions between the independent variables. The statistical significance (α) levels are indicated by asterisks: $p < 0.05$ (*), 0.01 (**), and 0.001 (***). If the significance threshold (for a main effect) was not exceeded, the lowest achieved level is reported (e.g., $p < 0.36$ in the case of a main effect of hand for cMTG). Abbreviations: H = hand; M = manuality; F = functionality; T = task; PES = partial eta squared; OP = observed power (computed using α). The analyses were performed with IBM SPSS Statistics for Macintosh v. 25.0.0.0, Armonk, NY: IBM Corp.

Table 3. ROI analysis results with interactions with control objects as a reference. Inputs for this analysis were parameter maps from the second level of the analysis (averaged for each participant), as referenced to non-tools (similarly to Figure 15), rather than control objects (for these results see Figure 12 and Table 2). Functional ROIs that were used to perform this analysis were obtained from the study by Przybylski and Kroliczak (2017). The regions were spherical masks of 5-mm radius, centered at peak voxels for the planning of functional grasps of tools contrasted with control objects. The table presents MNI coordinates of these voxels, their maximal *Z* values and results of the ROI analysis performed on the data from the current experiment (interactions with bimanual and unimanual objects). Here, as well as in the study by Przybylski and Kroliczak (2017) ROIs functionally defined for the right hand were used for extracting percent signal change for the right-hand condition in the current study (and *vice-versa* for the left hand). In other words, although locations of the two ROIs are provided in the table below, values that were subject to the ROI analysis were obtained separately for the right hand and left hand. Abbreviations of experimental conditions and statistical terms are described below the table.

		MNI coordinates							
Left hemisphere region	Hand	x	y	z	Peak Z value	Main effect of hand (right, left)	Main effect of manuality (uni-, bimanual)	Main effect of task (plan, grasp, exec.)	Interactions
Caudal middle temporal gyrus (cMTG) lateral occipital (LO) cortex	Right Left	– 48 – 42	– 66 – 72	– 2 – 4	4.2 4.37	0.12	*** PES = 0.43, OP = 0.94	** PES = 0.41, OP = 0.83	(H × M)* PES = 0.28, OP = 0.73
Anterior supramarginal gyrus (aSMG)	Right Left	– 54 – 52	– 34 – 34	38 36	5.42 5.15	0.68	** PES = 0.3, OP = 0.77	0.1	(H × M)* PES = 0.24, OP = 0.65
Caudal superior parietal lobule (cSPL)	Right Left	– 12 – 18	– 74 – 74	48 50	4.23 4.3	* PES = 0.26, OP = 0.7	** PES = 0.31, OP = 0.79	* PES = 0.33, OP = 0.7	(H × M) $^{p<0.085}$ PES = 0.14, OP = 0.4
Ventral premotor cortex (PMv)	Right Left	– 58 – 54	2 2	38 32	4.46 4.91	0.06	0.99	0.23	(T × M) $^{p<0.089}$ PES = 0.14, OP = 0.38
Dorsal premotor cortex (PMd)	Right Left	– 22 – 26	–14 – 14	64 56	5.26 4.67	* PES = 0.22, OP = 0.6	0.24	** PES = 0.48, OP = 0.92	(H × M) $^{p<0.12}$ PES = 0.11, OP = 0.32
Rostral middle frontal gyrus (rMFG) (right hand from inclusive contrast)	Right Left	– 36 – 36	36 36	30 30	2.75 4.07	0.47	0.27	0.73	–

Note. The goal of the ROI analysis performed here (after Kroliczak & Frey, 2009, and Przybylski & Kroliczak, 2017) was to test for differences and direction of amplitude (%) signal changes in conditions relative to the baseline brain state during performing tasks with non-tool objects. Variance of the signal within each ROI was explained by either the main effect of the factors, or interactions between the independent variables. The statistical significance (α) levels are indicated by asterisks: p < 0.05 (*), 0.01 (**), and 0.001 (***). If the significance threshold (for a main effect) was not exceeded, the lowest achieved level is reported (e.g., $p < 0.36$ in the case of a main effect of hand for cMTG). Abbreviations: H = hand; M = manuality; F = functionality; T = task; PES = partial eta squared; OP = observed power (computed using α). The analyses were performed with IBM SPSS Statistics for Macintosh v. 25.0.0.0, Armonk, NY: IBM Corp.

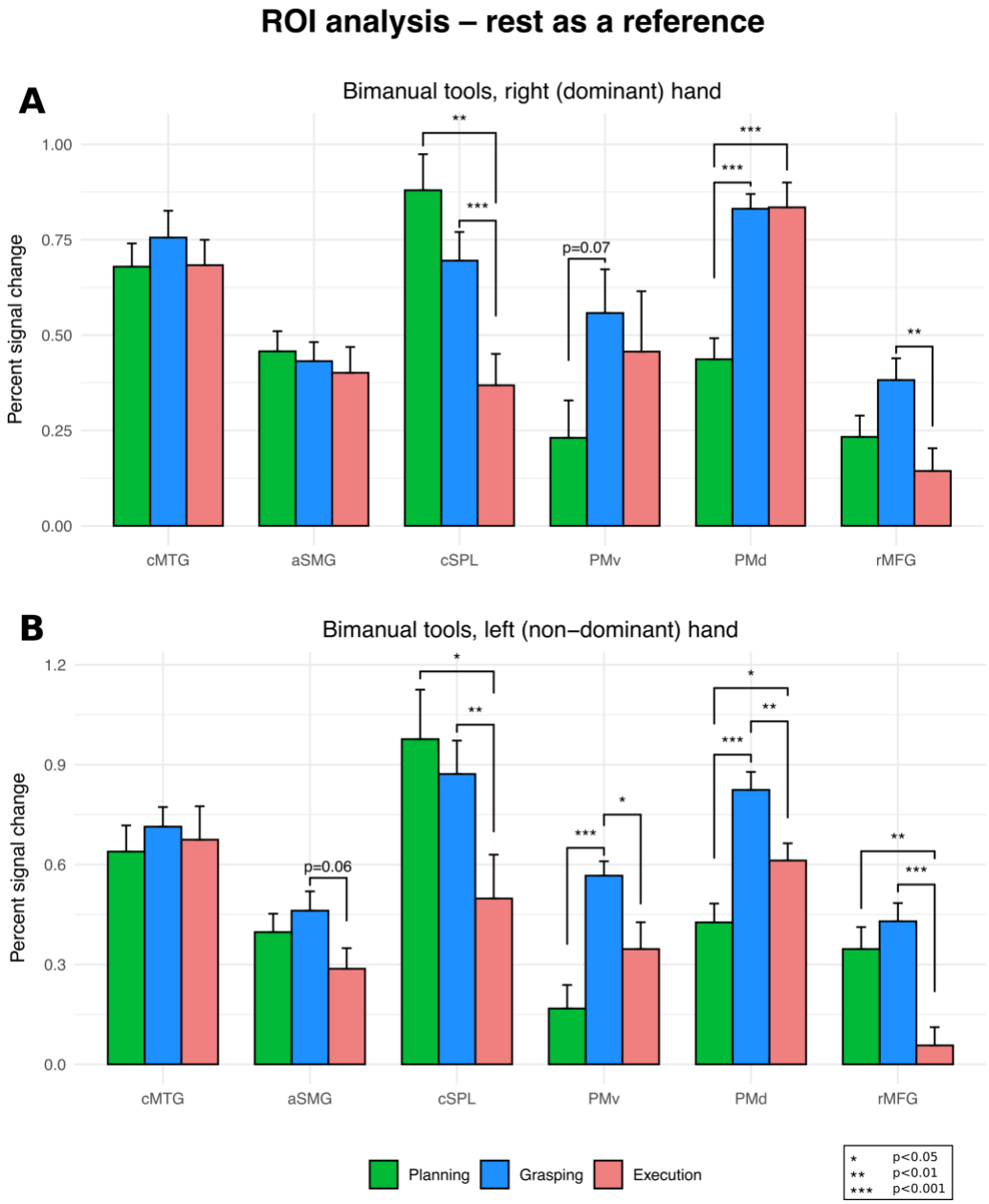

Figure 19. Percent signal change within regions of interest (ROIs) between particular phases of the task with rest periods as reference. Results presented in this figure are *de facto* post-hoc comparisons for the interaction: *hand* × *manuality* × *functionality* × *task*, however, restricted only to: *right/left* (both levels of the *hand* factor), *bimanual objects* (only one level of the *manuality* factor – bimanual objects), *tool* (only one level of object *functionality* – tools), and *plan/grasp/execute* (all three levels of the *task* factor). Within the *hand* factor, mean percent signal variations across different sites of PRN for different tasks are separated into right (dominant) hand (top panel, **A**) and left (non-dominant) hand (bottom panel, **B**). For each hand and for each ROI, three stages of the task were analyzed: planning functional grasps (green bars), performing functional grasps (blue bars), and executing the action with the tool in hand (red bars). One may notice that the regions differentiating best between *planning*, *grasping* and *execution* conditions are (regardless of the effector considered): cSPL, PMd and rMFG (with some trend for PMv in the case of the dominant hand, and aSMG for the non-dominant hand). Asterisks indicate the following levels of statistical significance (α): $p < 0.05$ (*), $p<0.01$ (**), and $p<0.001$ (***) (see also the legend in the bottom right corner of the graph).

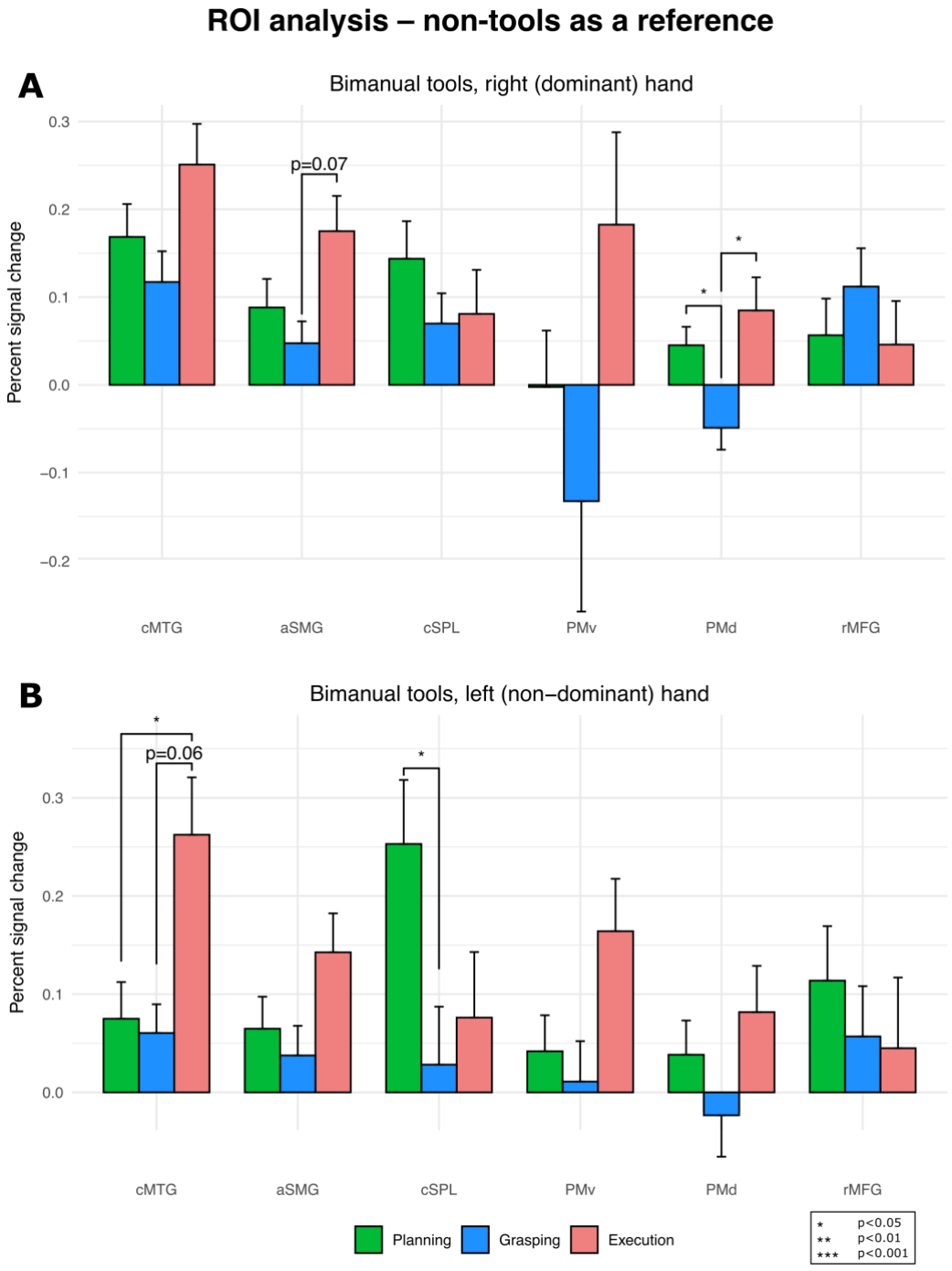

Figure 20. Percent signal change within ROIs between particular phases of the task with control objects as reference. Results presented in this figure are *de facto* post-hoc comparisons for the interaction: *hand* × *manuality* × *functionality* × *task*, however, restricted only to: *right/left* (both levels of the *hand* factor), *bimanual objects* (only one level of the *manuality* factor – bimanual objects), *tool* (only one level of object *functionality* – tools), and *plan/grasp/execute* (all three levels of the *task* factor). Within the *hand* factor, mean percent signal variations across different sites of PRN for different tasks are separated into right (dominant) hand (top panel, **A**) and left (non-dominant) hand (bottom panel, **B**). For each hand and for each ROI, three stages of the task were analyzed: planning functional grasps (green bars), performing functional grasps (blue bars), and executing the action with the tool in hand (red bars). For the right hand, only PMd seems to differentiate between phases of the task, with a trend in aSMG. In the case of the left hand, cMTG and cSPL are the most important regions for processing a particular phase of the interaction with a bimanual tool. Asterisks indicate the following levels of statistical significance (α): $p < 0.05$ (*), $p<0.01$ (**), and $p<0.001$ (***) (see also the legend in the bottom right corner of the graph).

3.2 Results of Experiment 2 – Additional experiment

The outcomes of the additional experiment with adjusting the grasp will be presented in this section. Although there were four conditions in this experiment: (1) inconvenient bimanual grasps, (2) convenient bimanual grasps, (3) inconvenient unimanual grasps, and (4) convenient unimanual grasps, here I will focus exclusively on the bimanual conditions – as the bimanual conditions were the most important from the point of view of this thesis. More detailed analyses are available in Appendix D to this work.

3.2.1 Inconvenient vs. convenient grasps of bimanual tools

The general, hand-independent effect of adjusting/swapping the acting hand for the functional grasp is visualized in Figure 21 below. This hand-independent result was obtained by averaging the outputs of higher-level analyses across both hands, utilizing fixed effects modelling, as implemented in FSL's FEAT program. Statistically significant differences within the left hemisphere were restricted to the visual cortex, namely prestriate area V2, and its immediate vicinity in *area prostriata* (the prostriate cortex; MMP notation: ProS). In the right hemisphere there were two significantly different clusters of voxels: one within the temporal association cortex (TA2), and the second within the middle-to-posterior insular cortex (MI to PoI2).

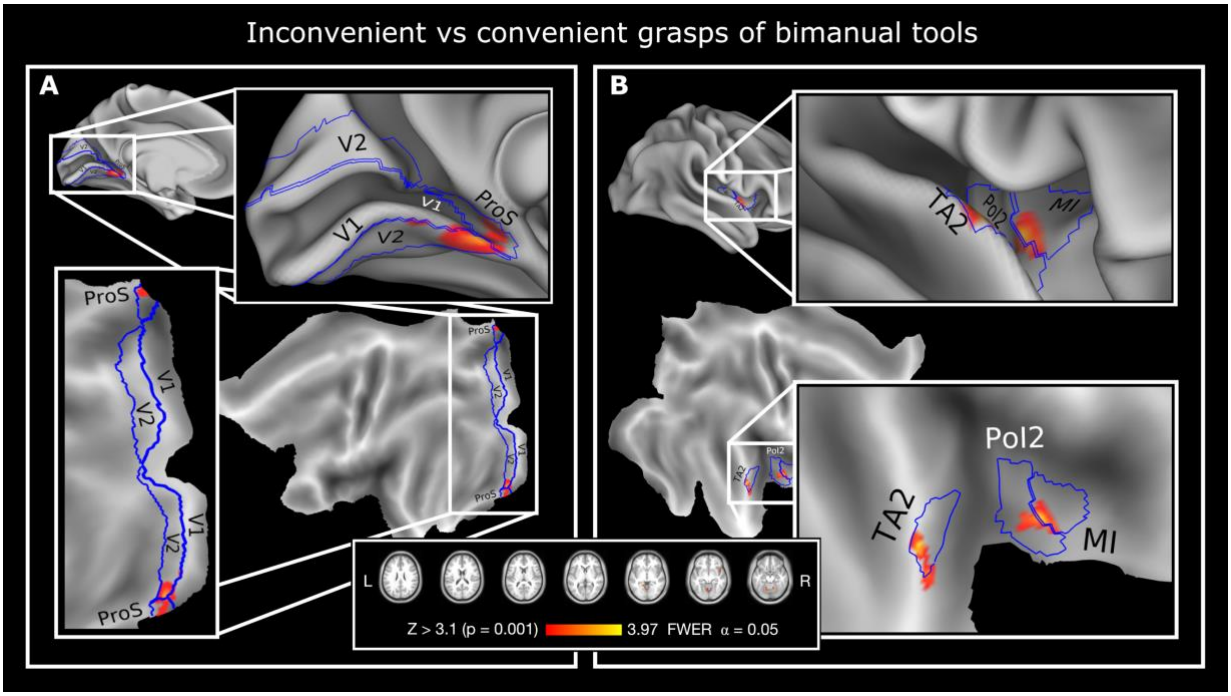

Figure 21. Adjusting inconvenient grasps of bimanual tools. Results for inconvenient grasps of bimanual tools, as compared to convenient grasps of bimanual tools. The results are presented here at the hand-independent level (averaged across hands with fixed effects), i.e., right-hand leading bimanual condition and left-hand leading bimanual condition were collapsed. In the left panel (**A**) results for the left hemisphere are presented, where only the activity within the medial visual cortex was observed. On the right (panel **B**), the right-hemisphere results are shown, with the significant clusters of activity present exclusively on the lateral surface of the cortex, i.e., in the temporal association area (part 2), and more in-depth in the right insula. Abbreviations : ProS – the prostriate cortex; V1 and V2 – visual areas 1 and 2; PoI2 – posterior insular cortex, area 2; MI – middle insular cortex; TA2 – the temporal association area 2 (see Glasser et al., 2016).

Chapter 4. Discussion

In the search for the neural substrates underlying interactions with bimanual tools, a three-phase paradigm with real objects was used in this dissertation in order to examine representations of planning, grasping, and using such a category of objects. In addition to a critical introduction of a scanner-friendly (non-ferromagnetic) 3D tools of real size, my paradigm consisted of three stages – planning, grasping, and using – devoted to different kind of interactions with bimanual (as well as unimanual) tools, which were perceived and acted upon by the participants in these disparate time intervals. While real objects were of course used in the past in neuroimaging work on tool-related behaviors (see, e.g.: Brandi et al., 2014; Hermsdörfer et al., 2007; Laimgruber et al., 2005; Singh et al., 2019; Styrkowiec, Nowik, & Kroliczak, 2019), there were only a few fMRI studies utilizing real tools with unrestricted upper hand movements in the context of a multiple-stage task. In fact, the introduction of the latter allowed me for an in-depth exploration of neural signals devoted to disparate tool-related cognitive processes. For instance, I was able to show that although SPL is crucial for grasp planning and grasping bimanual tools (as compared to unimanual tools) and for the planning of functional grasps of tools in general (bimanual and unimanual), SPL was not differentially invoked during the grasp phase when the two categories of tools were combined, and during the use of bimanual tools (when compared with using their unimanual counterparts).

First, my study revealed that the most critical effects which were specific to planning bimanual tool use are observed mainly outside of the traditionally defined praxis representation network (Figure 15A, and Figure 16A), so far typically associated primarily with the unimanual tool use (e.g., Kroliczak & Frey, 2009). The key cluster was located in the right hemisphere, and involved the entire area 7PC, as well as its more posterior vicinity of VIP of the superior parietal lobule. While the functions of these two areas are well recognized, with area 7PC being also regarded as the hub of the executive control network (e.g., Jung et al., 2017), these functions are primarily associated with the left-hemisphere processing. Additionally, Marangon and colleagues (2016) have demonstrated that right-hemispheric superior parietal lobule is engaged in processing of object complexity while performing haptic exploration of complex, as compared to simple objects (Marangon et al., 2016). In my study, the observed neural activity was exclusively right-lateralized and, in addition to multi-modal or amodal mechanisms implemented in this vicinity for representing movements in peripersonal space (e.g., movements towards the face, see Guipponi et al., 2013), it can be also associated with bimanual

coordination (see Serrien et al., 2006). The additional engagement of sensorimotor cortices also suggests that the key aspect of planning functional grasps of bimanual tools is intermanual coordination. Indeed, the analysis revealed that during the planning phase the initial bimanual movement sequences are being preprogrammed in 7PC and VIP prior to performing bimanual functional grasps.

Second, the importance of these two areas was corroborated in the subsequent grasping phase (Figure 15B and Figure 16B), wherein the neural processing reached the highest extent and amplitude during bimanual grasp performance. In the parietal cortex, this activity then involved both VIP, as well as LIPv. While the neural activity in LIP in general (whether ventral or dorsal) is thought to be effector-specific (Christopoulos et al., 2018), namely, it is associated with the control of eye movements, its contribution in my study was revealed largely at the hand-independent level during the grasping phase, suggesting greater contributions of eye-movement signals in the control of bimanual functional grasps. Moreover, the neural activity in the grasping phase was more widespread in the right hemisphere, and, in fact, involved the dorso-dorsal stream, extending from the V6/V6A complex (a part of the superior parieto-occipital cortex, SPOC; see Gallivan & Culham, 2015), via LIPv, VIP, 7PC, and sensorimotor cortices, through the premotor area 6d, and the abutting subdivisions of area 6mp and 6a of the right frontal cortex, also associated with increased attentional processing (Allan et al., 2019).

Third and finally, less neural engagement specific for bimanual tools was revealed across the cerebral cortex when bimanual tools were actually used, as compared to their unimanual counterparts. Interestingly, in addition to lower-level sensorimotor and visual processing, this activity involved area V3A – a visual motion-selective area (Nakhla et al., 2021; Tootell et al., 1997), indicating that the use of bimanual (vs. unimanual) tools generates more motion-related visual signals.

In the following sections these results will be discussed and my Discussion will involve revisiting theories of neural mechanisms underlying interactions with bimanual and unimanual tools in the light of the obtained results. The aim of my conclusion is to explain how, in more general terms, these outcomes may contribute to our understanding of the human motor cognition.

4.1 Planning functional grasps of tools

In accordance with previous praxis-related research, when participants planned functional grasps of tools – both bimanual and unimanual – mostly left-lateralized activity within the

tempo-parieto-frontal neural substrates, known as the PRN (praxis representation network) was elicited (Figure 8A and Figure 9; cf. Johnson-Frey et al., 2005; Kroliczak & Frey, 2009; see also Vingerhoets & Clauwaert, 2015; Przybylski & Kroliczak, 2017). However, what is specific about my outcomes is that, to the best of my knowledge for the first time, this effect was revealed while these interactions were planned for both real bimanual and unimanual tools used in one experiment, with the same number of stimuli from each class. In previous studies mainly unimanual tools and unimanual non-tool control objects were considered, instead. Furthermore, in my experiments functionally-matched pairs of bimanual and unimanual tools were used, so not only the number of bimanual and unimanual tools was the same, but also the function of these objects was equivalent. Thereby, the main experiment of my thesis revealed that most of the left-lateralized PRN nodes do not differentiate between bimanual and unimanual tools. Namely, the neural activity within these nodes is not exclusive to unimanual tools and some critical information related to bimanual tools – e.g., about their functions and the way they are used – is processed there, as well. Indeed, in the majority of PRN nodes, except for cSPL (and even SPL in general), the obtained signal changes were strongly left lateralized. Therefore, the theory predicting that skilled motor interactions with tools are represented in the left hemisphere for the majority of the population is strengthened by the empirical results described in this thesis. In other words, it turns out that the praxis representation theory is valid even for a wider range of functional objects than previously thought (Frey, 2007; Johnson-Frey et al., 2005; Kroliczak & Frey, 2009).

4.1.1 Planning of grasping bimanual vs. unimanual tools

When planning bimanual tool grasps was compared with planning unimanual grasps of tools, exclusively right-hemispheric activity within the sensorimotor and dorsal parietal areas was observed, with a cluster covering the whole area 7PC and its immediate vicinities (Figure 15A and Figure 16A). As mentioned above, 7PC is thought to be a hub for distributing information between executive control network and representation network (Jung et al., 2017). In the context of bimanual manipulations, bilateral activity within the superior parietal lobule was elicited when observation of bimanual actions was contrasted with observation of the movement of control objects (see Fig. 4 in Heitger et al., 2012).

Moreover, area 7PC is also a part of the dorso-dorsal stream of neural processing (Rizzolatti & Matelli, 2003), which is specialized in the on line control of actions. Interestingly, however, this primarily sensory-motor area was more active in the grasp planning phase in an earlier study from our laboratory (Przybylski & Kroliczak, 2017), suggesting that 7PC plays

a key role in grasp planning/preprogramming, by providing inputs to area aIPS, typically associated with grasp formation, regardless of whether functional or not. Moreover, the involvement of the 7PC parcellation was observed during haptic tool exploration (based on somatosensory rather than visual inputs), and the area was then re-activated during performance of functional grasps, even after the delay interval following haptic exploration (Styrkowiec et al., 2019). In none of the earlier studies were these interactions triggered by bimanual actions with tools, so given the current outcomes, this processing is not specific to unimanual tools. Furthermore, a presence of the 7PC engagement in the grasp planning phase clearly indicates that it contributes not only to online control of interactions with tools but also to their preparation.

4.2 Functional grasps of tools

Interestingly, when participants were grasping bimanual and unimanual tools, no activity was observed within dorsal SPL areas, including 7PC, when compared to control grasps (Figure 8B and Figure 10). This observation strengthens the notion that the contributions of 7PC is grasp related – as it disappears after the subtraction of a control grasp – not being specific to functional grasp.

During grasping bimanual tools additional neural activity was observed in the dorsal premotor regions – i.e., anterior part of 6a, s6-8, 6ma, and SFL – as compared to grasp planning, and this activity was located more anteriorly during grasping than during grasp planning. Conversely, no activity was observed within the ventral premotor cortex, typically associated with grasp programming (Cavina-Pratesi et al., 2007) and grasp execution in humans (Binkofski et al., 1998; Przybylski & Kroliczak, 2017). The contribution of the aforementioned superior frontal areas suggests either higher order contributions to functional grasp performance or just the need for dealing with variable affordances (such as size, and orientation in space) when functional objects are acted on (Sakreida et al., 2016; Johnson & Grafton, 2003). In both cases, it is expected that the processing would involve the dorso-dorsal stream.

Additional areas that were engaged during grasp execution (IFSa, a9-46v, 46, and 9-46d) were located more prefrontally within the middle frontal gyrus and inferior frontal sulcus, which also suggests more higher-order inputs to the control of bimanual and unimanual functional grasps (cf. Kroliczak et al., 2008).

Within the parietal cortices, only a cluster at the intersection of PF, PFm, IP2, and AIP was observed, which indicates that the contributions from the left inferior parietal cortex

involved in understanding of tool-related actions (e.g., Reynaud et al., 2016) are also needed during reaching and grasping, possibly because all aspects of such functional interactions with tools cannot be fully sequenced during the grasp planning phase alone. Finally, the neural activity extending from the caudal temporal cortex to lateral occipital areas was most pronounced in subdivisions PH, FFC, VVC, and VMV3, a vicinity which has been also associated with planning functional (though unimanual) grasps in our lab (Przybylski & Kroliczak, 2017; see also Cavina-Pratesi et al., 2007).

These results, for grasping as compared to grasp planning, suggest that the functional interactions with tools are preprogrammed at an earlier stage of task performance, namely during grasp planning, and these movement patters are then refined (their representations sharpened and more restricted) during tool grasping. In other words, the relevant representations of motor sequences required for performance of functional grasps are finetuned during grasping and given the imminent tool use phase can be further adopted. Indeed, according to some reports (e.g.: Johnson-Frey et al., 2005; or Haaland, Harrington, & Knight, 2000), this is how interactions with familiar tools should be processed within the neural circuitry (cf. Raś, 2019).

4.2.1 Bimanual vs unimanual grasps of tools

A direct comparison of bimanual vs. unimanual grasps of tools reaffirmed the importance of the SPL subdivisions, such as 7PC, as well as VIP and LIPv. Greater activity was, moreover, observed in bilateral sensorimotor cortices, and cingulate motor cortices (area 24dd), as well as in the right-hemispheric occipito-parietal V6/V6A complex (see Figure 15B and Figure 16B). As mentioned above, the involvement of the V6/V6A complex suggests that during grasping bimanual tools an additional on line processing has to take place, which is probably related to differential arm movement sequences for bimanual, as compared to unimanual grasping (see Gallivan & Culham, 2015). According to other reports, SPL (including 7PC) – and SPOC in particular (here restricted to V6/V6A), governs transforming object-related information into motor plans for the guidance of both arms, while an additional involvement of PMd is also needed in this process for fine-tuning hand orientation (see, e.g., Gallivan, McLean, Valyear, et al., 2011; and Monaco et al., 2014).

Thus, consistent with earlier studies, grasping bimanual vs. unimanual tools elicited the activity along all of the key regions of the dorso-dorsal stream of processing (Rizzolatti & Matelli, 2003), including V3A, V6/V6A, LIP/VIP, 7PC, up to area 6d. This suggests that the dorsal pathways are more engaged in ‘acting on’ an object, when grasping bimanual tools, as

compared to their unimanual counterparts (Johnson & Grafton, 2003). In other words, this shows that, indeed, the bimanual and unimanual tools used in my experiment were matched in terms of their functions, i.e., during grasping no differential activity was observed in the inferior parietal cortex – typically linked to 'acting with' objects. In other words, there was no difference in processing conceptual functional knowledge of tool use and pragmatics of an action between these two categories of functional objects. As a matter of fact, the same was the case during planning functional grasps of bimanual vs. unimanual tools.

4.3 Tool use

Using bimanual and unimanual tools involved a substantial bilateral brain activity spanning from the inferior frontal gyrus through the sensorimotor cortices and superior parietal lobule to the cingulate gyrus, as well as a large cluster located within the lateral temporo-parietal cortex to medial parts of the early visual cortex (Figure 8C). In accordance with previous reports, tool use elicited the left-lateralized activity in larger brain areas than a grasp/tool-use preparatory task (cf. Frey, 2007), and the results from grasp-preparatory processes and tool-use partly overlap. In addition to that, in my experiment I showed that this effect was revealed when bimanual tools were introduced to the experimental paradigm. These outcomes strengthen the notion that although tool-use requires widespread interactions between multiple temporo-parieto-frontal brain areas (Gallivan et al., 2013), the observed pattern of activity is consistently observed across different categories of functional objects (tools).

4.3.1 Bimanual vs unimanual tool use

Interestingly, when the activity invoked by using bimanual tools was compared with activity from using unimanual tools, only a small cluster in the dorsal sensory-motor cortex was revealed, as well as two additional, also smaller, clusters in the occipital lobe, one in the V3/V3A complex, and another within the calcarine sulcus (areas V1) extending to V2. Therefore, even after controlling (with non-tools) for the substantial differences in movement kinematics and lower-level visual features between bimanual and unimanual tools, significant differences were still found for using bimanual tools, as compared to their functionally-matched unimanual counterparts. These differences can be attributed to disparate requirements for sensorimotor and visuomotor control for bimanual tool-directed actions (Culham et al., 2006; Downey et al., 2019). I.e., bimanual tools are far more demanding in terms of sensori- and visuomotor processing than unimanual tools, and that is why greater increases in neural activity are observed in sensory-motor and visual cortices. Arguably, the way bimanual and unimanual

tools are embodied during brief functional use of such objects is different, as the recalibration of multisensory representations during tool use has been recently shown to be largely driven by visual cues, which clearly differ between bimanual and unimanual tools (Miller et al., 2017; see also Miller et al., 2019).

4.4 Previous results on bimanual actions and bimanual coordination

Although, as mentioned above, it has been established that functional grasp-preparatory processes take place mostly within the left hemisphere, the strength of this lateralization is debated. For instance, Vingerhoets and collaborators (2012) suggested that planning bimanual tool-use pantomimes is a good way of testing the strength of the lateralization of praxis skills between righthanders and lefthanders (Vingerhoets et al., 2012). The authors established that, regardless of handedness, the key regions engaged in processing bimanual tool-use pantomimes, as opposed to unimanual tool-use pantomimes, were premotor and posterior parietal cortices within the left hemisphere (both parts of PRN). Moreover, the right-hemispheric posterior parietal area significantly contributed to signal processing during coordinating bimanual pantomime of tools, as well. Therefore, while praxis skills are lateralized similarly for righthanders and lefthanders, for left-handed people bimanual tool-use pantomime has been more equally represented across both brain hemispheres.

Conversely, in the study by Heitger and colleagues (2012) contrasting bimanual vs. unimanual action observation showed no statistically significant differences (see the results for the main interaction in Heitger et al., 2012). Nevertheless, when bimanual action observation condition was contrasted with observation of the actions with non-dominant left hand, three clusters of significant brain activity have been revealed, namely, the left posterior MTG, right middle medial IPS, and a cluster in the right occipital cortex. The bias towards the right hemisphere, despite that the contralateral left-hand condition was subtracted, suggests that increased kinematic-related processing has to be performed for the observation of bimanual actions.

The results of my experiment, although focused primarily on the planning and grasping components of the interaction with tools, are to some extent consistent with outcomes obtained by the two previous neuroimaging studies on bimanual manipulation (Vingerhoets et al. 2012; and Heitger et al., 2012). First, direct comparisons between planning grasps of bimanual tools vs. unimanual tools, performed separately for each hand, revealed statistically significant effects only in the ipsilateral posterior parietal and sensorimotor cortices (partly consistent with

the results from Heitger et al., 2012). Interestingly, when the neural activity was collapsed across two hands, the only common clusters were found in the right SPL, emphasizing contributions from areas coding visuo-spatial processing for action performance. Correspondingly, when the control condition was accounted for, my analyses revealed similar sensory-motor and superior parietal regions within the right hemisphere that were specific for planning functional grasps of bimanual tools (as compared to unimanual tools); again, partly in line with results obtained both by Heitger and colleagues (2012), and Vingerhoets and collaborators (2012).

The fact that only sensorimotor and superior parietal cortices in the right hemisphere turned out to be significantly more engaged in processing of the bimanual tool category (bimanual vs unimanual) suggests that bimanual tools as more complex (they are often bigger, and have two handles or grasp points) require substantially more distributed and intensive neural processing than the functionally equivalent unimanual tools (see also: Frey, 2007; Shea et al., 2016). It is not surprising given the fact that these two kinds of tools are characterized by substantially different patterns of movement kinematics, with more refined coordination being required in the case of bimanual tools. Actually, both of these aspects (kinematics and coordination) are processed primarily within the sensorimotor cortices and superior parietal regions (Casellato et al., 2010).

There are several possible explanations for why during planning grasps of bimanual tools significant clusters of activity were observed exclusively within the right hemisphere (regardless of whether *rest* or *control* condition was used as a reference). One of the possibilities is that the handedness of the participants plays a role in how the brain processes bimanual objects. Right-handed participants have their contralateral (i.e., left) hemisphere dominant for deliberate motor control (Morecraft et al., 2013; however, cf. Begliomini, Sartori, Di Bono, Budisavljević, & Castiello, 2018; and Downey et al., 2019). Hence, in the case of bimanual coordination, which requires synchronizing activity between motor cortices in both hemispheres, processing the signal within the right SPL feeding the ipsilateral sensorimotor cortex is more demanding, thus it reaches the significance threshold. Yet, the increased activity observed for both hands was located exclusively in the right hemisphere, indicating that planning functional grasps of bimanual tools requires additional resources which are independent from motor-dominance. According to this view, the activity I observed can be associated with higher-level visuo-spatial and motor representations (e.g., preprogramming of coordinated responses of both hands in the same peripersonal space), which is definitely more than merely conveying simple motor signals to the muscles.

Interestingly, Serrien and collaborators (2003) established, based on the outcomes of their EEG experiment, that although the simple unimanual movements are governed primarily by the contralateral hemisphere, the bimanual coordination in right-handers is handled to the greater extent by the motor-dominant (left) hemisphere (Serrien et al., 2003). Although my results also show exclusively left hemisphere increases of neural activity during manual responses required for bimanual tool use, during the two phases preceding the actual tool use, i.e., planning bimanual grasps and bimanual grasping, this activity has been primarily lateralized to the right hemisphere (see, e.g., Figure 15 in the Results section above). Thus, extending previous studies on simple bimanual coordination, my research shows that the bimanual manipulation of tools is largely prepared within the right hemisphere, and only the subsequent performance of bimanual tool use is governed by the left hemisphere. These findings again emphasize the importance of having a multi-phase paradigm.

Another intriguing clue in my data is that the right-hemisphere activity elicited by planning grasps of bimanual tools suggests greater contribution of the allocentric representations to the preparation of bimanual grasps. The distinction between the two frames of reference: egocentric (with respect to the position of the body in space) and allocentric (external point/object-centered) is well established in the neuroscience literature (see, e.g.: Chen et al., 2014; Di Vita, Boccia, Palermo, & Guariglia, 2016; Galati et al., 2000; Milner & Goodale, 1993). However, theoretical analyses, simulations, and experimental data suggest that, in fact, all spatial representations can be explained solely in terms of egocentric frame of reference (Filimon, 2015). Indeed, a recent report showed that there are some common neural substrates for processing both egomotion-compatible and scene-compatible (triggered by relevant allocentric cues) optic flow signals (see Sulpizio, Galati, Fattori, Galletti, & Pitzalis, 2020). Nevertheless, the neural correlates for ego- vs. allocentric frames of reference remain separate to some extent. Moreover, the distinction between ego- and allocentric representations can be useful in understanding some more specific phenomena, such as the studied here planning of bimanual functional grasps directed towards bimanual tools. Hence, despite Filimon's observation that allocentric representations, most probably or to the greater extent, depend on egocentric ones, I will further treat these two frames of reference as separate concepts.

In their study, Galati and collaborators (2000) established experimentally the neural underpinnings of ego- and allocentric frames of reference (Galati et al., 2000). By asking their participants to determine the location of a stimulus with reference to either their own bodies, or an external object, they showed that although the right hemispheric fronto-parietal cortices were

activated by both conditions, egocentric processing required also inputs from the left hemisphere. Similarly, Massen and Sattler (2010b) performed a behavioral experiment on bimanual tool use in order to determine whether coordinative constraint dominance (either ego- or allocentric representations) depends on the frame of reference for bimanual movements (participant's body vs. an external cue; see Massen & Sattler, 2010b). The experiment confirmed that even for such a highly specific condition as using bimanual functional objects, ego- or allocentric representations are engaged in a different manner. What is also interesting about this study is that mixing both frames of reference (ego- and allocentric representations) resulted in reaction times about 50% slower than when movement was performed in either of the constraints.

The outcomes of my experiment are consistent with, but also extend, these behavioral results on bimanual coordination into the neuroimaging domain. Signal fluctuations within the right hemisphere during planning functional grasps of bimanual tools can be related to the external frame of reference, which is more important in this task, than in the case of unimanual tools. As the action progressed from grasp planning to grasp performance, the requisite object-related frame of reference (i.e., inputs from the right hemisphere), must be replaced by increasingly more important, hand-related (i.e., body-centered) coordinates – and the contributions from the left hemisphere are more and more evident.

Notably, independent of the brain hemisphere, the two visual streams of processing – dorsal and ventral – can be differently engaged in encoding allocentric vs. egocentric properties of objects. According to Goodale and Milner (1992), the processing within the dorsal stream focuses on egocentric information, while allocentric properties of objects are processed by the ventral stream (see also Brogaard, 2012). The fact that I observed mostly dorso-dorsal brain activity when interacting with bimanual tools suggests that planning, grasping and using bimanual tools is based strongly on egocentric properties of objects (tools in this case). Hence, the current data suggest that during bimanual interactions with tools, there is a division of labor between the right and left hemisphere dorsal streams. In this framework, the right hemisphere contributes to establishing appropriate body-centered response coordinates for the planning and guidance of functional bimanual grasps, and the left hemisphere ensures that the requisite coordinated response with bimanual tools already in hands is appropriately executed.

The model of the semantic system by Allport (1985) indicates that all things, including tools, are represented in a semantic architecture distributed across the cerebral cortex (Allport, 1985; Buxbaum & Saffran, 2002). In this theoretical framework, the features of an object also activate sensory and motor systems based on the action-related coding that is most critical

during the acquisition and processing of the information related to that object. My experiment revealed that the bimanual component of actions requires increased contributions from sensorimotor cortices, as compared with unimanual actions, which in turn suggests that bimanual responses require the orchestration of disparate kinds of processing, including proprioceptive, then tactile and motor information crucial for successful, functional interaction with bimanual tools.

Interestingly, the engagement of right superior parietal areas (indeed, bilateral parieto-frontal activity) was observed in ambiguous tool-use context, and for non-functional "*manipulative*" grasps (Natraj et al., 2013). Yet, for functional tool-use in the correct context – wherein both the functional object and action recipient were present – predominantly left parieto-frontal activity was observed. In my study, however, a context for bimanual tool use was not ambiguous but more complex and demanding. Thus counter to demands imposed for unimanual tool use in the Natraj and colleagues (2013) study, where all 23 objects were used in the context of their appropriate recipients (as in the "*One hand, two objects: …*" by Borghi, Flumini, Natraj, & Wheaton, 2012), any ambiguity in my study was introduced either by the additional target object or handle. A comparison of these outcomes shows that whether the additional object or part serves a function of a recipient or target is critical, and the inclusion of additional targets for bimanual coordination in experimental designs reveals the non-PRN related processing or mechanisms. Thus, without a proper control of the assignment of objects to the target recipient category, it might be impossible to create a reliable general theory explaining the neural underpinnings of interactions with tools, whether bimanual or unimanual.

Although in my experiment the number of trials with dominant vs. non-dominant hand was balanced, during planning bimanual grasps with the less skilled, non-dominant hand leading the action, the apparent increases in the right hemisphere activity might be additionally biased by greater demands for more deliberate control of the weaker hand, as well as the associated attentional demands. As Sirigu and collaborators (1996) showed, a damage to the left hemisphere impairs motor imagery with both hands, while right-hemispheric posterior parietal lesions disturb motor imagery only with the contralateral hand (Sirigu et al., 1996; see also: Buxbaum, Johnson-Frey, & Bartlett-Williams, 2005). It is, therefore, possible that during planning bimanual grasps of tools, the contralateral hand (the non-dominant, left hand, in the case of right-handed participants) engages more right-hemispheric resources than the dominant hand (regardless of whether the right or left hand is the *leading* one). Hence, while the contribution from both hemispheres is not eliminated, the greater right parietal and sensorimotor activity can to some extent be hand dependent.

4.5 Engagement of the parietal and temporal cortices in planning functional object-directed actions

Parietal and temporal brain regions play distinctive roles during performance of object-directed actions (see, e.g., Buxbaum & Saffran, 2002). Specifically, while knowledge about the action that will be performed with an object is represented in parietal regions, the function of this object is usually processed within the temporal cortex (e.g., Buxbaum, Veramontil, & Schwartz, 2000; Chen et al., 2016). However, it is disputed during which stage of the interaction with tools knowledge-related and function-related information is processed. With the three-phase experimental design it was possible to study the issue of a dissociation between object identity (i.e., what it is) and its function (i.e., what it is for) not only during action itself (the use of tools) but also during movement preparation (i.e., during grasp planning), as well as during grasping an object. In other words, the question was at which stage of neural processing, the divergent brain mechanisms for action knowledge and function knowledge can be distinguished for bimanual, as compared to unimanual tools.

As there were two general classes of objects in my experiment: tools and non-tool control objects, and participants were required to perform an action with both of these categories of objects, clearly, in order to properly grasp a tool, the information about its function has to be first accessed, then retrieved, and finally processed. This is not necessarily the case for the control objects, as control objects had no predefined function. Therefore, with the paradigm I utilized, it was possible to determine, first, where knowledge about the action as such (i.e., what to do with an object) is represented in the cerebral cortex; and second, what the neural underpinnings of knowledge on the function of an object and its proper grasp are (i.e., what the object is for). Moreover, by distinguishing further between two subclasses of objects – bimanual and unimanual tools and non-tool objects – it was possible to disentangle action and functional knowledge about unimanual objects, as opposed to bimanual objects. In other words, it was not only possible to determine whether action knowledge is represented differently from function knowledge, but also what the differences between the neural underpinnings of bimanual and unimanual actions are.

According to the *two-action system model* developed by Buxbaum (Buxbaum, 2017), tool-use ability is based on the interplay between the left-lateralized ventro-dorsal stream (manipulation knowledge) and bilateral dorso-dorsal system (sensory-motor mapping). The main experiment described in this thesis revealed that bimanual tool use is based on the mechanisms responsible for mapping sensory inputs to motor output (dorso-dorsal stream),

rather than on knowledge about how to skillfully manipulate this kind of functional object (ventro-dorsal stream). It is quite a surprising outcome, given the fact that previous reports on pantomiming bimanual tool use (Vingerhoets et al., 2012), as well as on observation of real actions with bimanual objects in conspecifics (Heitger et al., 2012), showed at least some contributions from middle to inferior parietal regions (i.e., IPL contributions for pantomiming in Vingerhoets et al., 2012; and IPS in observation in Heitger et al., 2012, respectively). This discrepancy can be explained by the fact that my task was more specific – not only real tools were used, but also the emphasis was put on the functional grasps of tools, i.e., on grasp planning and tool grasping. Participants were explicitly instructed to plan functional grasps, not the tool use action *per se* – as compared to previous experiments, where mainly the execution (i.e., tool use) phase was studied. It seems that the comparison between planning actions with bimanual and unimanual tools underlines primarily the sensory-motor characteristics of these two classes of functional objects. There is, however, a noteworthy difference between grasp planning and executing actions with the non-dominant hand, and that difference is observed in the caudal middle temporal gyrus, as revealed by the ROI analysis (visualized in Figure 20) – there is a difference between grasp planning and tool use. Such an outcome means that, at least to some extent, there are functional differences between bimanual and unimanual tools.

According to some other theoretical approaches, such as the one supported by the outcomes of an experiment by Bub and collaborators, the parietal cortex (more exactly: IPL) is associated with knowledge on how to manipulate objects (*manipulation knowledge*), while temporal cortices, especially their anterior parts (ATL), are considered a hub for semantic information about objects – *function knowledge* (see, e.g.: Bub, Masson, & Bukach, 2003; or Boronat et al., 2005). Studies with repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) by Ishibashi and colleagues seem to provide a strong empirical evidence supporting this distinction (Ishibashi, Lambon Ralph, Saito, & Pobric, 2011; Ishibashi, Mima, Fukuyama, & Pobric, 2018). However, in one condition, tDCS stimulation of the ATL demonstrated its partial engagement in processing object manipulation, while according to the distinction between the 'IPL – manipulation' and 'ATL – function' concepts, such ATL stimulation should not have an influence on object manipulation (see Fig. 4 in Ishibashi et al., 2018, results for "ATL (vs Sham)" in manipulation task).

The outcomes of my experiment also contribute to the discussion on the IPL-manipulation vs. ATL-function divergence, namely, across all three phases of the task – the grasp planning, grasping tools, and tool use – dorsal parietal regions, including medial IPS, were more engaged for bimanual, as compared to unimanual tools. It is not surprising, given

the fact that interactions with bimanual tools, which are generally more demanding in terms of manipulation, require more extensive knowledge on how to handle this kind of functional objects (i.e., it requires manipulation knowledge). Meanwhile, in terms of functionality, the bimanual and unimanual tools that I used were equivalent to each other (i.e., no activity within ATL was observed). In fact, functional correspondence between bimanual and unimanual objects was actually one of my goals while I was preparing the experiment (see *matching for functional purpose* in the Methods section).

4.6 Effectors and tool manuality

The ROI analyses that I performed also enabled to test the effects of hand (dominant or non-dominant) on functional grasps planning and performance. While previously it was established that praxis skills are processed at the hand-independent level (e.g., Kroliczak & Frey, 2009), I wanted to explore whether or not these findings can be extrapolated into bimanual actions, as well. Both ROI analyses types, with rest or control objects as reference, revealed that PMd significantly differentiated the signal for the hand factor (see Table 2 and Table 3 for details), and additionally, cSPL showed differential activity for the two hands but only when rest was used as reference. Thus, effector-specific processing within the dorsal-dorsal stream turned out to be an important factor for bimanual interactions with functional objects, which were the most critical aspect of my experimental design. This finding is in part consistent with previously reported outcomes (see, e.g., Begliomini et al., 2008), which also demonstrated specific grasping-related activity, but modulated by handedness of the participants (Begliomini et al., 2008). Although handedness itself is not a direct evidence for the dependence of the activity within the dorso-dorsal stream on the effector in right-handed participants, it may suggest that such a relation really exists (see, e.g., Króliczak, Gonzalez, & Carey, 2019). Moreover, Begliomini and colleagues found the hand effect for precision grip in the right hemisphere dorsal premotor cortex, while my ROIs were left hemispheric. This effect may depend on differential engagement of neural mechanisms underlying precision grips, as compared to the whole-hand, power grips of tool handles that were used in my study. In fact, it has been shown that precision grips and power grips are associated with different fMRI activity patterns (Ehrsson et al., 2000), which can also explain why for precision grips mainly the left hemisphere was active, while power grips engaged more the right hemisphere.

Representations of motor acts in the premotor cortex have been also shown effector-dependent in action observation paradigms, e.g., looking at a motor act performed with the

same effector engaged the same anatomical sector of the cortex (see Jastorff et al., 2010). It should be noted, however, that the levels of the effector factor in the study by Jastorff and collaborators were: hand, mouth, and foot, i.e., there was no distinction between hands. Presumably, the difference between the dominant and non-dominant hand would be far less pronounced than between either of the hands and mouth, or the hands and foot. Moreover, in my study the activity within PMd was observed in all phases of the action (grasp planning, grasping and tool use), as revealed by the ROI analysis. Meanwhile other authors usually do not differentiate between these three stages of actions towards tools. Therefore, the time intervals for particular phases (and in fact the whole action) tend to be shorter in these studies than in mine (it is most evident in comparison to Begliomini and collaborator's work, 2008). Finally, in my study real objects were used, while it is often the case that participants pantomime grasps or tool use, or are not performing grips *per se*, but rather observe other agents doing so (as in action observation paradigms; see, e.g., Jastorff et al., 2010). More in-depth studies on the differences between utilizing pantomime vs. real tool use in experimental paradigms can be found in works by the Hermsdörfer group (see, e.g., Brandi et al., 2014; Hermsdörfer et al., 2007).

Swinnen and colleagues (2010), conversely, investigated neural representations of effector-independence for coordination skills, and clearly identified common structures for ipsilateral hand-foot coordination task for left and right side of the body (Swinnen et al., 2010). They established that the neural substrates of these abstract motor acts are located within parietal-to-(pre)motor cortices, predominantly in the left hemisphere, however, with some inputs from the right hemisphere as well. These outcomes resemble what was revealed in my experiment, namely, the specificity of my paradigm might have emphasized the aspect of right-hemisphere transformations within parietal and premotor cortices.

Another important clue on the role of premotor cortices in neural representations of motor acts can be found in the work by Rizzolatti and collaborators (2014):

> "[…], *the premotor cortex encodes mostly motor acts, largely independent of individual movements, but still maintaining a certain somatotopic organization, congruent with that of the primary motor cortex.*"
>
> Rizzolatti, Cattaneo, Fabbri-Destro, & Rozzi, 2014

This rises the following question: does the premotor cortex encode motor acts performed with the dominant hand differently from non-dominant hand motor acts? From a certain perspective, movements with each effector separately can be treated as divergent classes of motor acts; yet

both of these classes fall into a more general category, i.e., *hand movement planning* and/or *execution*. Hence, in other words, it is a question at which level of processing motor acts (such as hand movements) are represented within the premotor cortices. Results of the analyses I performed showed, consistent with the *somatotopy* effects considered by Rizzolatti and collaborators (2014), that there is some evidence for the divergent representations for particular hands (dominant vs. non-dominant hand). To resolve this issue even further, in the future I will perform a multi-voxel pattern analysis, where spatial codependence can be accounted for, as well (as I did earlier, see Buchwald et al., 2018), which is not entirely possible with the univariate models utilized for the purpose of this dissertation.

There is some body of evidence that the lateralization of certain key cognitive functions, at least to some extent, depends on handedness, e.g.: self-body recognition (Morita et al., 2019), language (Biduła et al., 2017), and praxis (Kroliczak et al., 2011). Although handedness is hardly a conclusive factor triggering atypical functional lateralization (not to mention reversed lateralization of, e.g., language and spatial attention functions), a reverse pattern of left-to-right and right-to-left functional lateralization is more frequent in left-handed participants (Mandonnet et al., 2020; Mazoyer et al., 2014). Yet, it is widely agreed upon that planning sequences of learned manipulation movements typically engage the left hemispheric network of brain regions. It was also experimentally established that virtually the same regions are engaged in a hand-independent manner (Kroliczak & Frey, 2009; Przybylski & Kroliczak, 2017). Planning bimanual tool use can be considered as a boundary condition in the debate on functional lateralization, because these skilled bimanual movements, as defined for the scope of my thesis, should also involve the left-hemisphere areas, while at the same time the coordination factor is expected to engage the right hemisphere, which is specialized in spatial processing. Moreover, actions involving bimanual tools considered in my project are characterized within a particular time framework – spanning within second-scale time intervals. Hence, the degree of lateralization for planning bimanual tool use may differ, especially as a function of time where the nature of the interaction with a tool evolves – from *planning*, through *grasping*, to finally *using* a tool. Right-handed participants in my experiment most probably had typical functional lateralization: language and praxis in the left hemisphere, visuospatial and executive functions in the right hemisphere. In the light of my results, inputs from the right hemisphere – which plays a more important role in processing of visuospatial information – are more critical for performance of actions with bimanual tools (cf. a comparison to unimanual tools), and therefore, right SPL involvement is more than expected. Notably, these right-hemisphere contributions diminished as the action progressed from the grasp planning

(exclusively right-hemisphere advantage for bimanual tools) to grasping and using a tool (more and more inputs from the left hemisphere as well).

To sum up this section, both factors, the hands to be used, and whether the tool is bimanual or unimanual, seem to influence a distribution of neural activity across the cerebral cortex, and how it fluctuates in time. Regions most specialized in processing this kind of information are the ones situated along the dorso-dorsal stream (Rizzolatti & Matelli, 2003): superior parietal lobule, and dorsal premotor cortex (that will be more extensively discussed later on), with additional inputs from frontal areas, namely, from the rostral middle frontal gyrus (see Table 2). This suggests that planning and controlling bimanual manipulations with tools is more demanding for our cognitive system. Hence, the role of object *manuality* should not be marginalized in tool-related research.

4.7 When adjusting the grasp can be an issue

The activity within the insular cortex (see Figure 21), as revealed in the experiment on grasp adjusting, suggests that the grasp adjustment task in the context of bimanual coordination is related to the phenomena of learning, internalization and automated patterns of coordination (i.e., automatization of behavior; see Puttemans et al., 2005). Although the participants were acquainted with study procedures prior to the experiment, and had an opportunity to train grasp-adjustment actions for as long as they felt necessary, during the experiment further automatization processes took place. An alternative explanation is that adjusting the grasps of bimanual tools is largely based on highly automated motor programs, and when participants were adjusting the grasps they relied on "automation" of adjusting the grasp to the *convenience* of the leading hand. Noteworthily, the results presented in Figure 21 were obtained at the hand-independent level, and the *convenience* for the non-dominant hand was in some sense forced by the experimental procedure. Nevertheless, the significant clusters of activity were reveled, suggesting that the grasp convenience (adjusting the grasp) can be a factor in the results observed in fMRI studies.

No such effect was observed in the main experiment, which suggests that no significant grasp adjustments were required for either tools in general, or for bimanual tools, when compared to their functionally-equivalent unimanual counterparts. Moreover, lack of activity within the insular cortex during interactions with tools suggests that similar level of automation and learning can be attributed to bimanual and unimanual tools.

4.8 Intermanual actions and dorso-dorsal stream of neural processing

The engagement of dorsal visual areas, parieto-occipital sulcus and dorsal superior parietal lobule suggests that preprogramming of motor responses directed at bimanual tools elicits activity within the dorso-dorsal stream of processing (Rizzolatti & Matelli, 2003). It is not surprising, given the fact that "knowing" the exact object location in space at a given moment of time (for the subsequent control of movement towards it), i.e., its position, distance and orientation relative to the observer, is a more demanding task when it has to be performed with respect to two effectors, instead of one (see also: Jeannerod, 1988). Moreover, some of the tool stimuli used in my experiment were in fact two separate objects, which further emphasizes the role of the dorso-dorsal stream of processing for these stimuli.

Although the bilateral dorso-dorsal stream is known to be insensitive to object type (see: Binkofski & Buxbaum, 2013; Rizzolatti & Matelli, 2003; and Styrkowiec et al., 2019), the results of my experiment show that signal fluctuations within this pathway of neural processing were significant even when control objects were used as a reference. It means that certain aspects of processing within the dorso-dorsal stream can still be tool-specific, at least when it comes to bimanual manipulation.

The problem I addressed in my thesis may also contribute to what is known about the theory of affordances (Gibson, 1977; Osiurak et al., 2017). What was specific about the stimuli used in my experiment is that while bimanual and unimanual tools were matched for their functional purpose – they afforded the same action – at the same time these two categories of tools required almost completely different sets of movements to be orchestrated in order to perform the particular action. Importantly, as emphasized several times before, a key aspect of the bimanual tool-action performance is the requirement of *intermanual* coordination, which, in turn, is known to depend on interhemispheric communication (see, e.g., Swinnen, 2002). The grasp planning phase was particularly important from the perspective of the theory of affordances, as bimanual and unimanual tools afforded the same function, while the actual grasp that was planned substantially differed. Thus, the outcomes of my experiment can provide an answer to the question about to what extent tool affordances are *stable,* and whether these affordances *vary* depending on the context.

Stable affordances are derived from unchanging, invariant features and characteristics of objects which we are about to interact with. This is a binary relation, where on one side we have these objects, and on the other there is our organism that can interact with these objects (Borghi & Riggio, 2015). In other words, stable affordances allow us to interpret the objects'

offers – given that object properties are rather invariant in time and space, e.g., the size of an apple does not change depending on its location (whether it is close to us or far away; see, e.g., Jeannerod, 1994). On the other hand, variable affordances refer to temporary object features that vary in time and space. Following the same example – an apple can be located in different places in space (e.g., on a tree or on the table before us), and it can be positioned in different orientations, which entails diverse actions and motor acts that have to be performed, e.g., to grasp this apple (Borghi & Riggio, 2015).

Neuropsychological studies localize brain functions related to stable affordances in ventral parts of the dorsal stream of processing (the dorso-ventral stream), while variable affordances seem to be processed within the dorso-dorsal stream (see, e.g.: Young, 2006; Borghi & Riggio, 2015 after Borghi & Riggio, 2009; for the meta-analysis see also Sakreida et al., 2016). Thus, the variable affordances are closely related to the real-time control of actions towards objects. During planning bimanual grasps of tools mostly the dorso-dorsal stream was engaged (i.e., variable affordances were processed), which may suggest that the brain was preparing for the subsequent online control of grasping action. Indeed, bimanual tools require more visuo-spatial transformations to be taken into account than unimanual tools, when preparing tool grasps. Almost complete lack of activity within the dorso-ventral stream suggests that both bimanual and unimanual tools were related to the same stable affordances, which makes sense, given that an attempt was made to match stimuli in pairs, based on the corresponding functions of bimanual an unimanual tools. In this case, what was a "stable" property across these two categories of tools (bimanual and unimanual) were their functions, which were essentially very similar. It is worth noticing that aSMG, which is a part of the dorso-ventral stream, was close to reaching the significance threshold for grasping vs. using bimanual tools when the right hand was the leading one in the ROI analysis (see Figure 20A; see also aSMG in Figure 19B for a similar effect for the left leading hand). This suggests that there may be a difference in what bimanual tools afford, as compared to unimanual tools.

Assuming that what Gibson (1986) meant in his theory was that affordances are almost exclusively egocentric phenomena (a user-object relationship), it seems that affordances alone are not enough to explain how tool use and functional grasps are prepared in the brain (see: Orban & Caruana, 2014; Osiurak, 2013). Another factor to be considered is an allocentric relationship – the relationship between a tool and a recipient object – that is a kind of a "second-level affordance".

In the meta-analysis on 70 neuroimaging studies on tools, it was observed that activation patterns for recognition and naming tools largely overlap (Ishibashi et al., 2016). Thus, these

two conditions were merged together into a more general category of "tool identification", which subsequently was contrasted with signal fluctuations elicited by actions towards tools (i.e., with the brain activity from motor task studies). This contrast revealed that bilateral occipito-temporal cortices are more active during identifying tools, whereas left PMd, SPL and anterior cingulate gyrus were specific for action retrieval. According to the authors, such results are yet another evidence to strengthen the classic two-pathway theory (Ungerleider & Mishkin, 1982; and Goodale & Milner, 1992). The paradigm I utilized in my experiment is a serious candidate for contributing to Ishibashi's et al. (2016) results, since there are clearly dissociated phases for "identification" (the initial stage of the *planning* phase) and motor actions with tools (*grasping* and *using* tools). The results I obtained support the notion that bimanual and unimanual tools share the same neural resources for identity retrieval, as no differences were observed in areas commonly associated with processing object identity, i.e., neither in the inferior parietal (Borra et al., 2017; Kristensen et al., 2016; Lanzilotto et al., 2019), nor in the temporal cortices (Chen, Snow, Culham, & Goodale, 2017; Orban & Caruana, 2014).

Additionally, one could presume that the fact that during grasp planning participants had to choose whether to use left or right hand could lead to interhemispheric competition in posterior parietal cortices or in the superior parietal cortex (indications towards that can be found in the work by Fitzpatrick et al., 2019). That actually was not the case in my experiment, as participants were explicitly trained and instructed which hand to use, hence, there was no free hand choice in this paradigm. Thus, any inputs from the parietal sites, whether unilateral or bilateral, should be attributed to the aspect of bimanuality of the presented stimuli and, at most, to the phenomena of interhemispheric communication (collaboration), not to the interhemispheric competition.

4.9 Mechanical reasoning and a hierarchy of processing

As previously mentioned, the direct comparison between bimanual and unimanual objects yielded no striking differences within PRN, as it was confined mostly to the sensorimotor and superior parietal cortices in the main experiment (*plan-grasp-use* paradigm, Figure 15), and to middle-to-inferior insular and temporal association cortex within the right hemisphere in the additional experiment (*adjusting grasp*, Figure 21). The fact that, in general, the brain is preprogramming functional grasps similarly for bimanual and unimanual tools, may be an argument for the validity of the mechanical reasoning theory (Osiurak & Badets, 2016). According to the concept of mechanical reasoning, neural simulations of actions for different

classes of tools are more of an *ad hoc* nature. This is contrary to the manipulation knowledge hypothesis which advocates that there are motor plans being pre-stored in the brain (prior to performing an action) which are then used in actions with tools (Buxbaum, 2017; Buxbaum & Kalénine, 2010).

On the other hand, the gesture engram theory, which is one of the possible interpretations of the manipulation knowledge hypothesis, claims that different sensorimotor memories are being evoked for different kinds of habituated actions. My experiment revealed different patterns of neural activity in sensorimotor cortex and superior parietal lobule for bimanual tools – as compared to unimanual tools. This can be treated as direct evidence that different motor programs that can potentially be stored in somatosensory cortices, may require privileged access to right hemisphere resources for bimanual, as compared to unimanual tools. During planning actions with these objects, the putatively pre-stored motor memories would be retrieved, and, based on these memories, motor programs are prepared (may even be simulated) before the onset of an action. In some sense, the distinction between the mechanical reasoning and manipulation knowledge approach comes down to the question where the hubs for motor control would be located within the brain. Moreover, there is also a question on which tool-category level sensorimotor memories would be generated – are they generated for tools as such (in general, e.g., regardless of whether bimanual or unimanual), for particular classes of tools (categories, e.g., bimanual, unimanual), or even for individual tool exemplars (e.g., a hammer, scissors, etc.)? A discussion that follows will attempt to provide answers to these questions, based on the outcomes of my experiment, in the context of the studies reported in the literature.

Another important piece that was missing from the debate is motor learning, which was clearly stated by Baxbaum (2017):

> "[…] *a critical missing piece in the O + B account* [i.e., in the mechanical reasoning hypothesis, Osiurak & Badets, 2016] *is how sensory-motor actions can be simulated when there is no stored sensory-motor representation of ever having performed the action before. Most influential accounts specifying "internal models" for the purpose of action prediction explicitly describe mechanisms for* ***learning and tuning*** *these sensory-motor models (e.g., Friston, 2011; Wolpert & Ghahramani, 2000), and the O + B account glosses over this important point*".
>
> Buxbaum, 2017

There is a growing piece of evidence that not only motor learning occurs, which seems trivial from the point of view of modern neuroscience (besides studies by Buxbaum and collaborators, see also a review by Wolpert et al., 2011), but also that motor memories contain very detailed representations of tool-related actions, such as controlling specific locations on tool (possibly for analyzing the potential places to grasp a tool; see Proud et al., 2019). From that perspective, it seems more likely that, in fact, there are different sensorimotor memories for bimanual and unimanual tools stored in the brain.

One of the possible explanations of my outcomes in the light of Buxbaum's model – called "Two Action System framework" – is that bimanual and unimanual tools, at least to some extent, share the same portion of sensorimotor memories (Buxbaum, 2017). However, the differences between bimanual and unimanual tools were revealed primarily in the somatosensory cortex, which suggests that for bimanual tools these memories, i.e., motor patterns, are more complex. In such a vain, tool use actions were previously shown to modulate processing within somatosensory cortices, i.e., the sensorimotor system has to compensate for the motor capacity increases when a given hand is used (see: Miller, Longo, & Saygin, 2019). Hence, it is possible that bimanual tools require more of such compensation, as bimanual tools clearly change the physical and spatial characteristics of the hand – actually both hands – by increasing the capacity of the body far more than unimanual tools (e.g., compare a unimanual intrenching tool with a bimanual shovel).

Yet another important notion about the results presented in my thesis is that during the planning phase the neural activity was more extensive than during the subsequent grasping phase, when tool grasps were compared with non-tool grasps. The bulk of neural processing during grasping tools was observed in the more anterior parts of the frontal cortices and more posteriorly in parietal, as well as in the temporo-occipital brain regions (as compared to grasp planning). This suggests that both the actual movements and the overarching action goals must be preprogrammed earlier, during grasp planning, and these movement patters are then sustained, in order to be used during grasping tools. In other words, the relevant representations of motor sequences required for skillful tool use are first accessed or even tuned during planning to be implemented later on during grasping. In fact, according to some reports (e.g.: Johnson-Frey et al., 2005; or Haaland, Harrington, & Knight, 2000), this is how interactions with familiar tools are processed within the neural circuitry.

Correspondingly, more anterior processing in the frontal lobe suggests that some portion of higher level of processing is also required during planning grasps of bimanual tools. This argument is consistent with a notion that rMFG is engaged in the control of complex

movements. This is likely achieved by the mechanisms of *maintenance and manipulations of movement representations* – as it was suggested that the working memory is involved in such mechanisms (see Buxbaum, Shapiro, & Coslett, 2014, after Haaland et al., 2000). Moreover, according to the meta-analysis by Caspers and colleagues (2010), frontal regions – especially Brodmann Area 44 (BA 44) – are part of both the *action observation* network (AON), as well as various *action imitation* networks (Caspers et al., 2010). However, more detailed analyses revealed that more rostro-dorsal portions of the frontal cortices (BA 45) are more engaged in *observation* aspects, while increase in neural activity while *imitating* an action are reported in caudo-ventral vicinities of the frontal lobe (in BA 44). In line with previous studies on the distribution of activity within PRN (Kroliczak & Frey, 2009; Przybylski & Kroliczak, 2017), my experiment revealed planning-specific contributions from the more rostro-dorsal frontal areas (including rMFG). These areas are also associated with *action imitation* – see Fig. 7 in the aforementioned work by Caspers and collaborators (2010). This is not surprising given the fact that representations very similar to these of action imitation had to be accessed by the participants in my experiment while interacting with tools. Furthermore, Schumacher and D'Esposito (2002) showed that the dorsal prefrontal cortex (in the vicinity of rMFG) plays an important role in selecting a proper response to the external stimuli (Schumacher & D'Esposito, 2002). These results were later corroborated and extended by subsequent reports on that subject by the same, as well as other groups (see, e.g.: Poldrack et al., 2005; Ridderinkhof, Van Den Wildenberg, Segalowitz, & Carter, 2004; Schumacher, Elston, & D'Esposito, 2003). This may suggest that my task, initially meant to reveal the divergent neural contributions for two kinds of objects (tools and non-tools) during movement preprogramming, also involved the component of selecting the adequate response to the presented stimuli: *grasp-to-use* (in case of tools) vs. *grasp-to-transport* (when interacting with control object). As a matter of fact, the latter may also be related to brain activity accompanying *grasp-to-pass* task (see, e.g.: Jax & Buxbaum, 2010; Osiurak, Roche, Ramone, & Chainay, 2013; Squires et al., 2016; Valyear et al., 2011). Another possible interpretation of my results, in the context of *grasp-to-move* or *grasp-to-use* distinction, can be found in the report by Lee and collaborators (2018). In this work, the authors postulated the existence of two divergent temporal and spatial mechanisms for *grasp-to-move* and *grasp-to-use* actions (Lee et al., 2018). As a matter of fact, this interpretation is in line with the classic "two-route" approach (Goodale & Milner, 1992) and a more recent Two Action System Plus model (Buxbaum, 2017).

4.10 What more can bimanuality tell us about motor cognition

Tool-use is one of the most complex behaviors that, at this level of complexity, is most specific to our species. Over the decades, several theories were proposed to explain what brain mechanisms are engaged in handling functional objects, and how a disruption of these mechanisms influences human behavior. In the present work I provided insights into some of these theories that were relevant from the point of view of the phenomena which I studied, i.e., planning functional grasps of bimanual tools. There are, however, plenty of open questions that are yet to be answered and theories to be validated in the context of bimanual tool use. What was of little concern in this work is how bimanual tools are incorporated in body schema and whether bimanuality is the feature that significantly alters the way tools are represented in our cognitive system. For instance, Cardinali and colleagues (2016) studied how sensory-motor constraints and morphology of a tool alters movement kinematics during and after period of using tools (Cardinali et al., 2016). They showed that sensory-motor constraints imposed by the tools were more important for incorporating these tools into body representation than the function of these tools. The question arises: does the same apply to the functionally-equivalent bimanual and unimanual tools? Perhaps the assumptions about motor control, that hold for unimanual tools, should be altered or extended for their bimanual counterparts? A separate study would have to be designed and performed in order to provide an answer to this question.

Although, as I mentioned earlier, the neural underpinnings of bimanual action observation have already been studied, it still remains unknown how these phenomena can be explained in different inference frameworks. For instance, Ondobaka and Bekkering (2013) proposed a conceptuo-perceptual model based on Bayesian-inference for explaining what brain mechanisms underlie recognition of others' actions (Ondobaka & Bekkering, 2013). According to this account, the main component for recognizing behaviors of other agents is the interplay between purposeful objects and perceptuo-motor plans of movements towards (reaching) and with these objects (grasping, manipulating). The authors showed that movements and movement planning are partly dependent on observer's conceptual expectations (Ondobaka et al., 2012). Nevertheless, as neuropsychological evidence suggests, a conceptual system (knowledge about the world) and perceptuo-motor system (movement specification) are in fact two distinct modules. It is yet to be established whether this conceptuo-perceptual framework can provide formal scaffolding for explaining the differences in phenomena regarding actions with bimanual as opposed unimanual tools in terms of Bayesian computational model.

4.11 Limitations of my experiments

During planning the experiment, I was aware of some of the shortcomings of the procedure I was preparing. Some of them could be addressed by performing additional analyses, others, unfortunately, would require separate studies to resolve doubts associated with them. Now I will briefly present some of these issues and will attempt to discuss potential criticism concerning the experiments that I performed.

First and foremost, although the factorial design is a powerful technique to disentangle intertwined conditions, it requires strict balance in the nature of the factors, as well as their strength. Although I made my best in order to come up with a proper control condition for the experiment, it still may be disputed whether transporting cylindrical wooden rods is a satisfying control for tool manipulation. In my defense, I shall note that using these stimuli has one general advantage over more refined controls such as natural branches – they do not have any obvious function as such. That is why I finally decided on using as simple control objects as possible – wooden elongated cylinders that afford grasping, but indicate no particular function, such as: pointing, raking, scratching, etc., which can be the case for branches.

Second, as it was noted in the Methods section, the bimanual experimental stimuli could be further divided into separate categories, based on, e.g.: whether they are *symmetrical* or not (i.e., used in the same manner regardless of the dominance of one of the hands); whether it is a single solid object to be used bimanually, or there are two detachable objects; or whether a tool object can be placed in one central location of the workspace (e.g., mortar, rakes), or it has to be put in a different way that is more convenient for grasp performance (while lying in the scanner; e.g., hammer and chisel, sweeper and dustpan). I am well aware that separate, detailed analyses could reveal how much variance is explained by each of these factors, however, as it was not in a direct scope of this work, these contrasts were not run and are not described in this dissertation. For now, I would say that regardless of the subclasses of these stimuli, I did observe an effect specific to planning grasps of bimanual tools, thus providing at least partial evidence for the distinctiveness of bimanual tools as such. Furthermore, one could argue that, especially in the case of *detachable* bimanual tools, there would be differences in signal processing based on the visual hemifield. As said before, experimental stimuli were balanced across hands for the number of trials the *functional* part of bimanual tool (e.g., broom) was on the left or right side of the participant (and vice versa for the *supporting* dustpan part). Moreover, according to a recent case study report by Medina, Jax and Coslett (2020), potential parietal disparities in activity during non-action periods can be in fact caused by perceptual

processing, not by the *action* component *per se* (such as action planning; see: Medina, Jax, & Coslett, 2020).

Finally, despite my best efforts, and despite utilizing cutting-edge technology, studies on spontaneous interactions with real tools are still far from the satisfying experimental ecology (strict paradigms, laboratory conditions, scanner environment, headsets and attachable medical devices, etc.). Nevertheless, recent efforts on setting the boundaries between imagined, pantomimed and real tool use actions are very impressive. The experiment described in this dissertation is an attempt to meet the requirement of ecology, as participants interacted with real tools, additionally including bimanual tools, which play a crucial role in our everyday life, and which were missing from previous experiments.

Conclusions

The study described in this dissertation revealed that, counter to the initial expectations, the critical neural substrates underlying interactions with bimanual tools were located primarily outside of the praxis representation network. In addition to corroborating that the substantial part of neural processing associated with preparing functional grasps of bimanual and unimanual tools takes place during the grasp planning phase, my study demonstrated that the grasping phase invoked vital mechanisms, arguably even more important for interactions with bimanual tools. The greater engagement of the right superior parietal lobule suggests that tool complexity processing and bimanual coordination are the key components of the bimanual tool-related actions. The distribution of processing along the dorso-dorsal stream, spanning across both hemispheres during grasping, is an important piece of evidence supporting two notions: the interhemispheric communication is essential for effective right-hemisphere visuospatial, as well as left-hemisphere egocentric processing underlying motor coordination when 'acting on' bimanual tools with a view to functionally using them. Of course, the bulk of the 'acting with' processing would still depend on the praxis representation network of the left hemisphere. These results contribute to the tool-related theoretical frameworks, developed primarily in the context of unimanual tool use. My outcomes uncover both the neural areas and their inherent cognitive mechanisms making it possible for humans to interact not only with unimanual but also more complex bimanual tools.

Summary

Bimanual actions are the cornerstone of human evolution, and bimanual tool use is an essential part of our everyday life. The goal of this dissertation was to investigate the neural mechanisms underlying interactions with bimanual tools, which require substantial intermanual coordination associated with complex visuo-spatial processing. To this aim, two functional magnetic resonance imaging (fMRI) experiments were designed and performed, in which twenty right-handed participants interacted with real tools and control objects, either with the right or the left hand leading a performed action. In line with previous research on neural bases of functional tool use, a three-phase paradigm was utilized in order to examine representations of planning, grasping, and using bimanual vs. unimanual tools. The main experiment I carried out revealed that the most critical effects which were specific to planning bimanual tool use were observed mainly outside of the traditionally defined praxis representation network, i.e., a set of areas for the control of skilled manual actions, so far typically associated with the unimanual tool use. Bimanual tools, as compared to their functionally-matched unimanual counterparts, involved more the right superior parietal lobule and somatosensory cortices across all phases of the task, which suggests that the key aspects of interactions with bimanual tools are tool complexity and intermanual coordination. Moreover, during grasping bimanual tools additional brain regions along the dorso-dorsal stream of neural processing were engaged, corroborating the need for more demanding online control of bimanual actions. All in all, these results emphasize the importance of the intermanual coordination in preparing bimanual actions with tools, as well as the increased sensorimotor and visuomotor processing for this category of tools. Among a few contributions of this study to the field of neuroscience is, therefore, a characterization of the neural underpinnings and mechanisms underlying functional interactions with bimanual tools.

Streszczenie

Umiejętność działań oburęcznych stanowi kamień milowy w ewolucji człowieka, a dwuręczne użycie narzędzi jest kluczowym aspektem naszego codziennego funkcjonowania. Celem niniejszej dysertacji było zbadanie neuronalnych korelatów planowania działań z użyciem narzędzi dwuręcznych, które wymagają koordynacji między dwoma rękoma, przy udziale zaawansowanego przetwarzania wzrokowo-przestrzennego. Aby osiągnąć ten cel, przygotowane i wykonane zostały dwa eksperymenty z wykorzystaniem funkcjonalnego obrazowania rezonansem magnetycznym (fMRI), w których dwadzieścia zdrowych osób badanych zostało poproszonych o wykonanie zadań z prawdziwymi narzędziami dwuręcznymi i jednoręcznymi, oraz przedmiotami kontrolnymi, z prawą bądź lewą ręką wiodącą realizację danej czynności. Bazując na wcześniejszych badaniach neuroobrazowych nad użyciem narzędzi, dla określenia reprezentacji neuronalnych działań z narzędziami dwuręcznymi, w porównaniu z narzędziami jednoręcznym, do paradygmatu wprowadzono trzy fazy: planowanie funkcjonalnego chwytu, chwytanie i użycie narzędzi. Eksperyment główny, który przeprowadziłem, pokazał, że kluczowe efekty specyficzne dla interakcji z narzędziami dwuręcznymi obserwowane były poza siecią reprezentacji praksji, tj. kontrolującą wyuczone zdolności manualne, a dotychczas utożsamianą głównie z użyciem narzędzi jednoręcznych. Krytycznym komponentem w kontekście przygotowania działań z narzędziami dwuręcznymi nie są zatem zdolności praksyjne, a poziom skomplikowania narzędzi, przetwarzanie wzrokowo-przestrzenne oraz koordynacja między rękoma. Ponadto, w trakcie chwytania narzędzi dwuręcznych zaobserwowano również zwiększoną aktywność w grzbietowo-grzbietowym strumieniu przetwarzania neuronalnego, co oznacza większą potrzebę kontroli działań dwuręcznych w czasie rzeczywistym. Podsumowując, otrzymane rezultaty podkreślają wagę koordynacji między rękoma już na etapie przygotowania oburęcznych, funkcjonalnych chwytów narzędzi, a także większe wymagania co do przetwarzania sensomotorycznego oraz wzrokowo-ruchowego w przypadku tej kategorii przedmiotów. Jednym ze znaczących wkładów mojego badania do neuronauki poznawczej jest zatem scharakteryzowanie neuronalnego podłoża i mechanizmów stojących za interakcjami z narzędziami dwuręcznymi.

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Appendix A. Dictionary of abbreviations

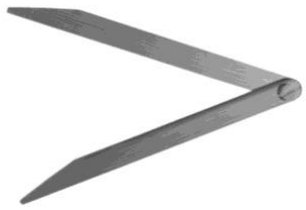
aIPS	anterior intraparietal sulcus
AON	action observation network
aSMG	anterior supramarginal gyrus
ATL	anterior temporal lobes
BA	Brodmann area
BOLD	blood oxygen level dependent
cMTG	caudal middle temporal gyrus
cSPL	caudal superior parietal lobule
DLPFC	dorsolateral prefrontal cortex
EEG	electroencephalography
fMRI	functional magnetic resonance imaging
IPS	intraparietal sulcus
ITG	inferior temporal gyrus
LOC	lateral occipital complex
MI	middle insular cortex
MFG	middle frontal gyrus
mmIPS	middle medial intraparietal sulcus
MMP	multi-modal parcellation (see Glasser et al., 2016)
MRI	magnetic resonance imaging
MT/MST	middle temporal visual area/medial superior temporal area
MTG	middle temporal gyrus
MVPA	multi-voxel pattern analysis
OC	occipital cortex
PoI2	posterior insular cortex, area 2
PMd	dorsal premotor cortex
PMv	ventral premotor cortex
PRN	praxis representation network
ProS	prostriate cortex
RDBM	role-differentiated bimanual manipulation
ROI	region of interest
rmANOVA	repeated-measures analysis of variance

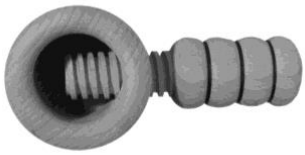
rMFG	rostral middle frontal gyrus
rTMS	repetitive transcranial magnetic stimulation
tDCS	transcranial direct current stimulation
SMA	supplementary motor area
SMG	supramarginal gyrus
SPOC	superior parieto-occipital cortex
TMS	transcranial magnetic stimulation

Appendix B. Stimuli used in the experiments

The table on the two following pages presents all stimuli used in the experiment. Refer to table caption for additional information.

Supplementary Table 1. Stimuli used in experiments, matched for their functions. Uni- and bimanual objects that were presented to and subsequently grasped by participants. Note, that my main goal was to account for the *function* factor, i.e. the two classes of tools were matched for the purpose they were supposed to serve. Control objects had no function *per se*, in the case of wooden rods was to grasp it and move from one place to another. Emphasized text in brackets below action names are expressions for these activities in Polish. 12 pairs of tools and 1 pair of control objects are presented in this table (26 objects in total). The table continues also on the next page.

No.	Action	One-handed object	Two-handed object
1	**chopping** (in Polish: *siekanie*)		
2	**cutting** (*cięcie*)		
3	**drilling** (*wiercenie*)		
4	**hammering** (*uderzanie*)		
5	**raking** (*grabienie*)		
6	**rolling** (*wałkowanie*)		

No.	Action	One-handed object	Two-handed object
7	**screwing** (*wkręcanie*)		
8	**spreading** (*smarowanie*)		
9	**stirring** (*mieszanie*)		
10	**squeezing** (*wyciskanie*)		
11	**twisting** (*odkręcanie*)		
12	**whisking** (*ubijanie*)		
13.	**transporting action** control objects		

Appendix C. Orders used in the experiment

Supplementary Table 2. Main experiment orders 1-3. The first three pseudorandomized orders used in the main experiment described in this dissertation. Another 2 orders from the experiment and one training order are presented in the table on the following page.

MAIN ORDER 1	MAIN ORDER 2	MAIN ORDER 3
mortar	control unimanual	control bimanual
pierogi maker	REST	control unimanual
REST	cookie cutter	control bimanual
control unimanual	churn	REST
REST	REST	plunger
meat mallet	control bimanual	control unimanual
control unimanual	REST	REST
nut cracker	control unimanual	rake unimanual
control bimanual	REST	REST
REST	rolling pin	sweeper and dustpan
box	control bimanual	kitchen knife
rake unimanual	hedge clippers	control bimanual
REST	REST	butter knife
kitchen knife	lemon squeezer	lemon squeezer
REST	plunger	hammer and chisel
herb knife	control unimanual	REST
rake bimanual	control bimanual	control unimanual
screw driver	sweeper and dustpan	meat mallet
hammer and chisel	REST	cookie cutter
control bimanual	corkscrew	REST
control unimanual	compass	churn
REST	scissors	REST
stirrer	meat roller	rake bimanual
control bimanual	butter knife	herb knife

Supplementary Table 3. Main experiment orders 4-5 and training order. Fourth and fifth pseudorandomized orders used in the main experiment described in this dissertation.

MAIN ORDER 4	MAIN ORDER 5	MAIN ORDER 6 (training)
control unimanual	scissors	nut cracker
screw driver	control unimanual	screw driver
REST	REST	control bimanual
control bimanual	control bimanual	control unimanual
compass	herb knife	sweeper and dustpan
mortar	control unimanual	REST
REST	REST	control unimanual
hedge clippers	control bimanual	rake bimanual
rolling pin	stirrer	meat roller
box	lemon squeezer	control bimanual
control unimanual	REST	REST
control bimanual	kitchen knife	control bimanual
REST	churn	REST
control unimanual	cookie cutter	mortar
scissors	REST	REST
stirrer	control unimanual	butter knife
nut cracker	hedge clippers	rake unimanual
REST	REST	REST
control bimanual	meat mallet	compass
meat roller	plunger	stirrer
REST	mortar	REST
corkscrew	control bimanual	rolling pin
REST	REST	control unimanual
pierogi maker	hammer and chisel	corkscrew

Supplementary Table 4. Block orders of an additional experiment.

BLOCK 1	BLOCK 2	BLOCK 3 (training)
Bimanual	Control (Bimanual)	Unimanual
Control (unimanual)	Unimanual	Control (Bimanual)
Unimanual	Bimanual	Bimanual
Bimanual	Unimanual	REST
REST	Bimanual	Bimanual
Bimanual	REST	Unimanual
Unimanual	Bimanual	Control (unimanual)
REST	Control (unimanual)	Unimanual
Control (Bimanual)	REST	REST
Bimanual	Bimanual	Bimanual
Control (unimanual)	Control (unimanual)	Unimanual
REST	REST	Control (Bimanual)
Unimanual	Control (Bimanual)	REST
Control (Bimanual)	Unimanual	Bimanual
Unimanual	REST	Control (unimanual)
REST	Unimanual	REST

Supplementary Table 5. Stimuli used in an additional experiment.

Unimanual	Bimanual
Corkscrew	Compass
Rake unimanual	Rake bimanual
Screw driver	Nut cracker
Stirrer	Mortar
Cookie cutter	Lemon squeezer
Pierogi maker	Box
Plunger	Churn

Appendix D. Supplementary analyses

D1 Supplementary analyses for Experiment 2 (adjusting grasps)

The additional analyses of the Experiment 2 (adjusting the grasps) are described in this supplementary section. Two detailed hypotheses were tested on the data acquired during this experiment: one of them regarded adjusting either bi- or unimanual grasps, the other hypothesis involved only unimanual tools. Results for adjusting grasps exclusively for bimanual tools, as well as regardless of tool type and hand, are presented in the "Results" section of this thesis.

D1.1 Inconvenient vs. convenient grasps of tools (regardless of tool type) with a hand factor included

Contrasting *inconvenient* and *convenient* grasps of tools revealed that, when tools either bimanual or unimanual were passed/swapped to the right leading hand, the following brain structures were engaged in this process: one, a large cluster in right-hemispheric sensorimotor cortices, extending from premotor (multi-modal parcellation, MMP areas 6mp and 6d) to post-central regions, extending from the superior parietal lobule (area 7PC) dorsally, to PFt ventrally.

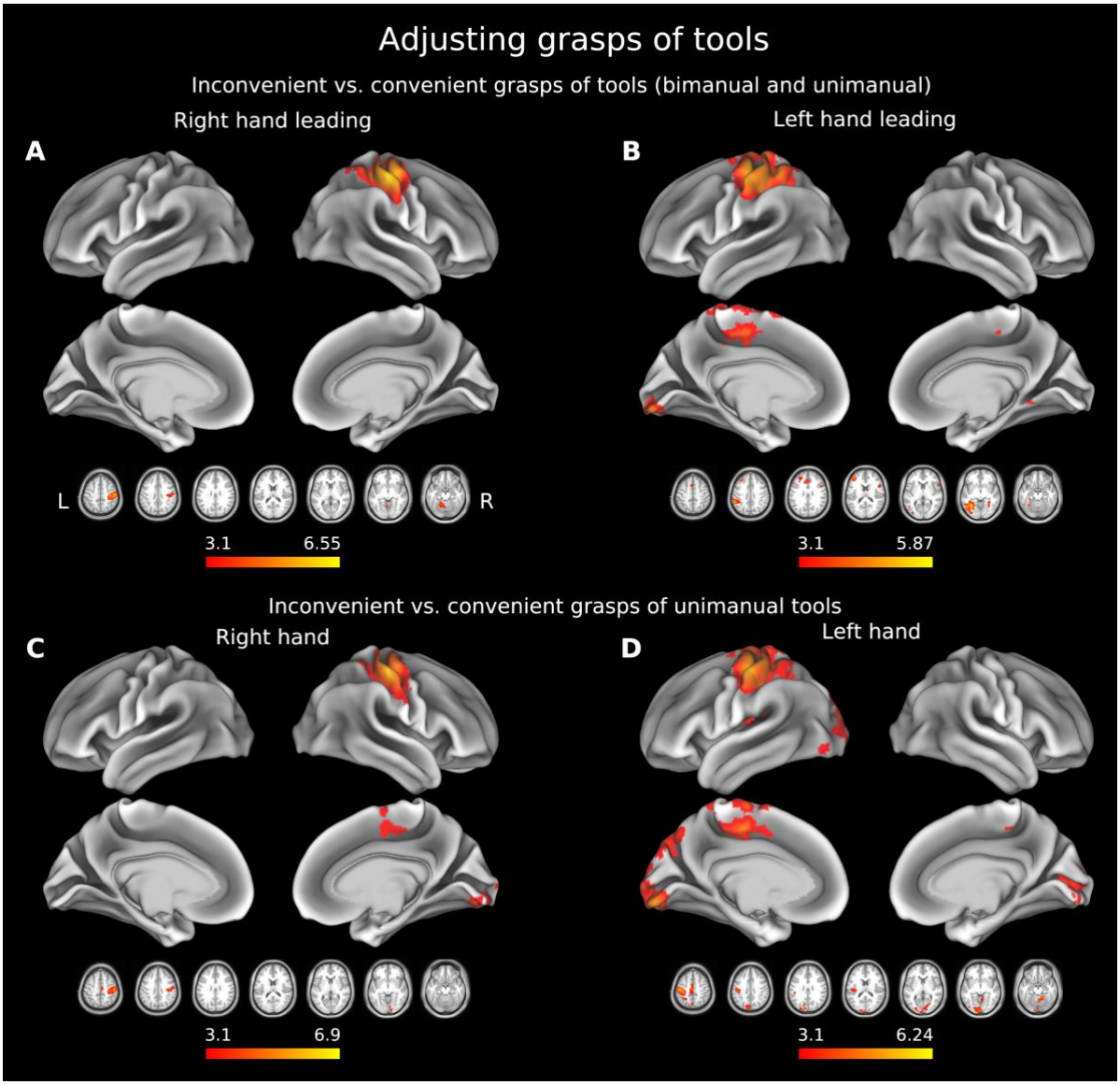
When the left hand was the leading one (or object had to be placed in this hand prior to using it), a very similar pattern was revealed in the left hemisphere, i.e., the network consisted of: premotor and sensorimotor areas (e.g., 6a, 6d, and 6mp; 7AL, and 7PC), as well as posterior partial contributions from area VIP, LIPv, and LIPd. Additional clusters in the left hemisphere were identified in the cingulate motor area (24dd), dorsal visual areas V1 to V4, and two small isolated clusters in the right hemisphere, one in anterior part of V2 and the other in superior part of area 24dd.

D1.2 Inconvenient vs. convenient grasps of bimanual and unimanual tools with a hand factor included

Inconvenient vs convenient grasps of unimanual tools with the right (dominant) hand elicited right-hemispheric brain activity within lateral (MMP: 6mp and 6d to 7PC) and medial (area 24dd) parts of the sensorimotor cortices, as well as in the ventromedial visual cortex (V1 to V4), as depicted in the Supplementary Figure 1C.

When inconvenient and convenient grasps with the left (non-dominant) hand were compared, a strongly left-lateralized brain activity was observed. Within the left hemisphere the following regions were engaged: premotor cortices (6mp and 6d), medial to dorsal

sensorimotor areas (24dd, 4 to 5L and 7PC), opercular areas 1-3 (OP1-OP3), dorsomedial part of the supramarginal gyrus (PFcm), within the vicinity of the parieto-occipital sulcus (POS2 and DVT), and in the visual cortex (V3 to V1). In the right hemisphere, the activity was restricted to the vicinity of the calcarine fissure (the primary visual cortex, V1), an additional dorsal cluster in the visual areas (at the border between V2 and V3), and a small cluster in the cingulate motor area (24dd). For these results see the Supplementary Figure 1D.



Supplementary Figure 1. Adjusting inconvenient grasps of tools. Results of the block experiment where participants had to adjust the *inconvenient* grasp after being given the tools not to the hand with which they were supposed to perform the action.

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